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CONTENTS

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ICTERUS NEONATORUM: ITS INCIDENCE AND CAUSE

BY

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Introduction

In spite of the frequency of icterus neonatorum and the work done to elucidate the problems connected with it, there still remains much divergence of opinion regarding its incidence and pathogenesis. Estimates of the incidence vary from 40 to 80 per cent. of the newborn. Since the detection of jaundice is influenced by many factors, such as the vascularity of the skin and the nature of the light in which the observation is made, and since there are several definitions of jaundice, such varying estimates are not surprising.

Icterus neonatorum has been ascribed to excessive haemolysis of the blood, to immaturity of the liver, to increased viscosity of the bile, and to the breakdown of the mother's blood in the placenta. The hypothesis that the jaundice was hepatic in origin has been replaced by one that it is caused by excessive haemolysis. Since bilirubin is a product of the breakdown of haemoglobin, all jaundice may be said to be the result of haemolysis, but the evidence of excessive haemolysis as a cause of icterus neonatorum is inconclusive.

During the past year, in the course of biochemical and haematological investigations of haemolysis, there occurred an opportunity to study newborn babies, and an investigation of icterus neonatorum was undertaken, (1) to determine the incidence, (2) to try to detect any difference in the rate of haemolysis in jaundiced and non-jaundiced infants, and (3) to seek evidence of impairment or immaturity of liver function.

Material and Methods. The children investigated were born in the maternity department of the Radcliffe Infirmary, Oxford. Foetal blood was collected from the umbilical cord before pulsation had ceased (from the umbilical vein by venepuncture, and from the artery after cutting but before ligation). Children's blood was obtained by venepuncture of a scalp vein or by incision of the skin of the heel Blood was collected in tubes containing heparin, and pipettes used for taking blood were washed through with liquid heparin.

Haemoglobin was estimated by Haldane's technique, using a standard colour tube calibrated at the National Physical Laboratory. Reticulocytes were counted by the wet film technique. Plasma proteins were estimated by micro-Kjeldahl technique (Howe, 1921). Plasma bilirubin was estimated by the Thannhauser and Andersen method (1921). Faecal bilirubin was estimated by a modification of Hunter's method (1930). Takata-Ara reaction was performed by Ragins' technique (1934). Faecal urobilin was detected by Schlesinger's test (1903). Fragility of red cells was measured by Creed's technique (1938).

Incidence of Icterus Neonatorum

The diagnosis of icterus neonatorum was made on the basis of a hyperbilirubinaemia in the cord blood or post-natal blood of an infant otherwise normal. This criterion was taken because the plasma bilirubin level is a more objective and accurate standard than the observation of jaundice, that is, the yellow coloration of the skin and mucous membranes, since the observation of this condition is much influenced by the degree of hyperaemia and the nature of the light in which the examination is made. As the coloration is due to infiltration of the tissues by bilirubin, any patient with an excess of bilirubin may be considered the subject of icterus neonatorum, whether or not the yellow coloration is present.

It is proposed to define ' hyperbilirubinaemia ' as a plasma bilirubin level greater than 1 mg. per cent. This arbitrary level is chosen because it is unusual to find in a normal adult a plasma bilirubin level above this figure. No figures are available for the plasma bilirubin levels of a large series of young infants, but in all the patients studied in this

* We deeply regret that, just as we were going to press with this issue, the death of Professor Leonard Findlay was announced.

investigation the plasma bilirubin concentration was below 1 mg. per cent. at the age of two weeks.

Seventy-three infants were observed once during the first ten days of life, and of these, thirty-four (46 per cent.) had plasma bilirubin levels between 1·2 and 20·0 mg. per cent. at the time of examination. In twenty-eight of the infants the levels were 2·0 mg. per cent. or above, and eighteen showed jaundice. The absence of a definite bilirubin level at which jaundice appears was probably due to the difficulties of observation mentioned above. However, all infants (eight in number) who had a plasma bilirubin level above 5 mg. per cent. showed icteric discoloration of the skin and mucous membranes. The observations in this series of infants are recorded in fig. 1.

Hyperbilirubinaemia in foetus. Not only do a large proportion of infants have hyperbilirubinaemia during the early days of life, but also many normal infants are born with a high plasma bilirubin and, though not jaundiced, are nevertheless by our criterion undoubted examples of icterus neonatorum. This point is important and should be considered in any discussion of the etiology of the condition.

The plasma bilirubin concentrations of the cord blood in 110 infants was measured (fig. 2); in 68 cases (62 per cent.) a hyperbilirubinaemia was observed. However, the plasma bilirubin of the cord blood never reached the high levels seen after birth. It will be seen that, as previous workers have observed, there is some relation between the foetal hyperbilirubinaemia and the post-natal rise of plasma bilirubin, but in contrast with the results of Ylppö (1913) and Hirsch (1913), our figures fail to reveal an absolute correlation. Of eighteen infants in whom the cord blood bilirubin was over 2 mg. per cent., four did not develop jaundice. Nevertheless, it seems that in general the higher the level of foetal bilirubin, the greater is the chance of the development of jaundice (table 1, p. 73).

Relation between plasma bilirubin level and maturity of foetus. No correlation exists between cord plasma bilirubin concentration and the maturity of the foetus (fig. 2). This constitutes evidence against Ylppö's view that there is in the foetus no means of excretion of haemoglobin derivatives, for, if this were so, it would be expected that plasma bilirubin concentration would rise with the age of the foetus. Possibly haemoglobin derivatives are excreted before birth through the placenta.

Plasma bilirubin concentration during the neonatal period. In sixteen infants the level of bilirubin was determined in the cord blood and in the blood at intervals for the first twelve days after birth (fig. 3). There are three groups of cases. In group A (eight infants, 50 per cent.) the plasma bilirubin level rose noticeably, reaching a maximum of from 3 to 9·4 mg. per cent. on the third to ninth day and usually declining rapidly thereafter to a figure below 1 mg. per cent. by about the tenth day. Jaundice was seen only in this group. In group B (six infants, 37 per cent.) the foetal bilirubin level was below 1 mg. per cent., and during the first few days of life there was only a slight rise, never exceeding 2 mg. per cent. and returning to a normal level by the tenth day. Though none of these patients showed jaundice, nevertheless by our standard three must be considered cases of icterus neonatorum. In group C (two infants, 13 per cent.) the foetal blood showed hyperbilirubinaemia which diminished after birth, the normal levels being reached by the first and the eighth days.

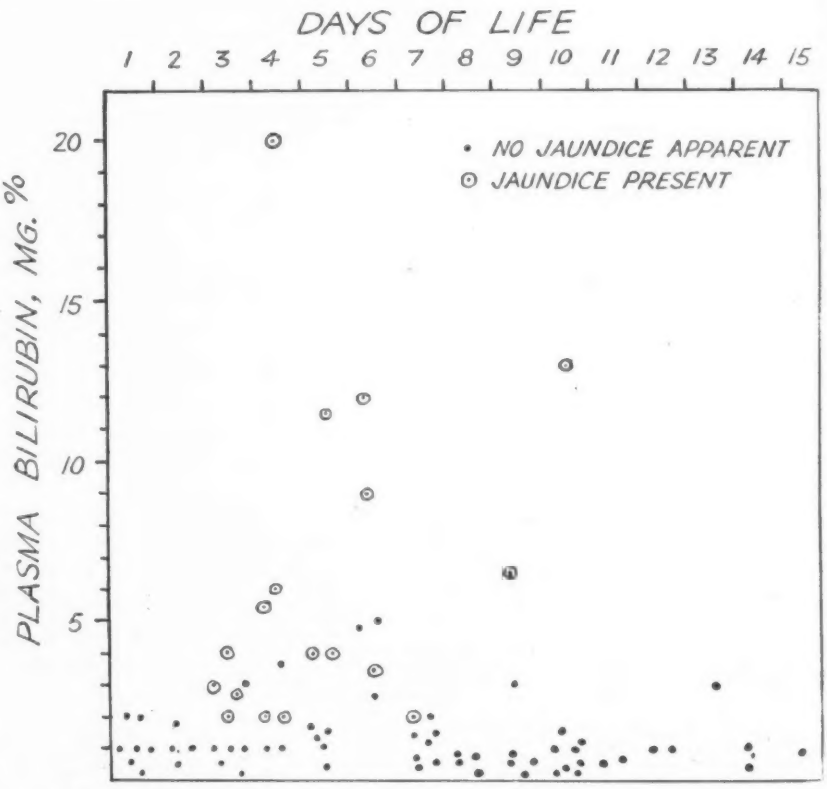

FIG. 1.—Plasma bilirubin in newborn infants during first two weeks of life.

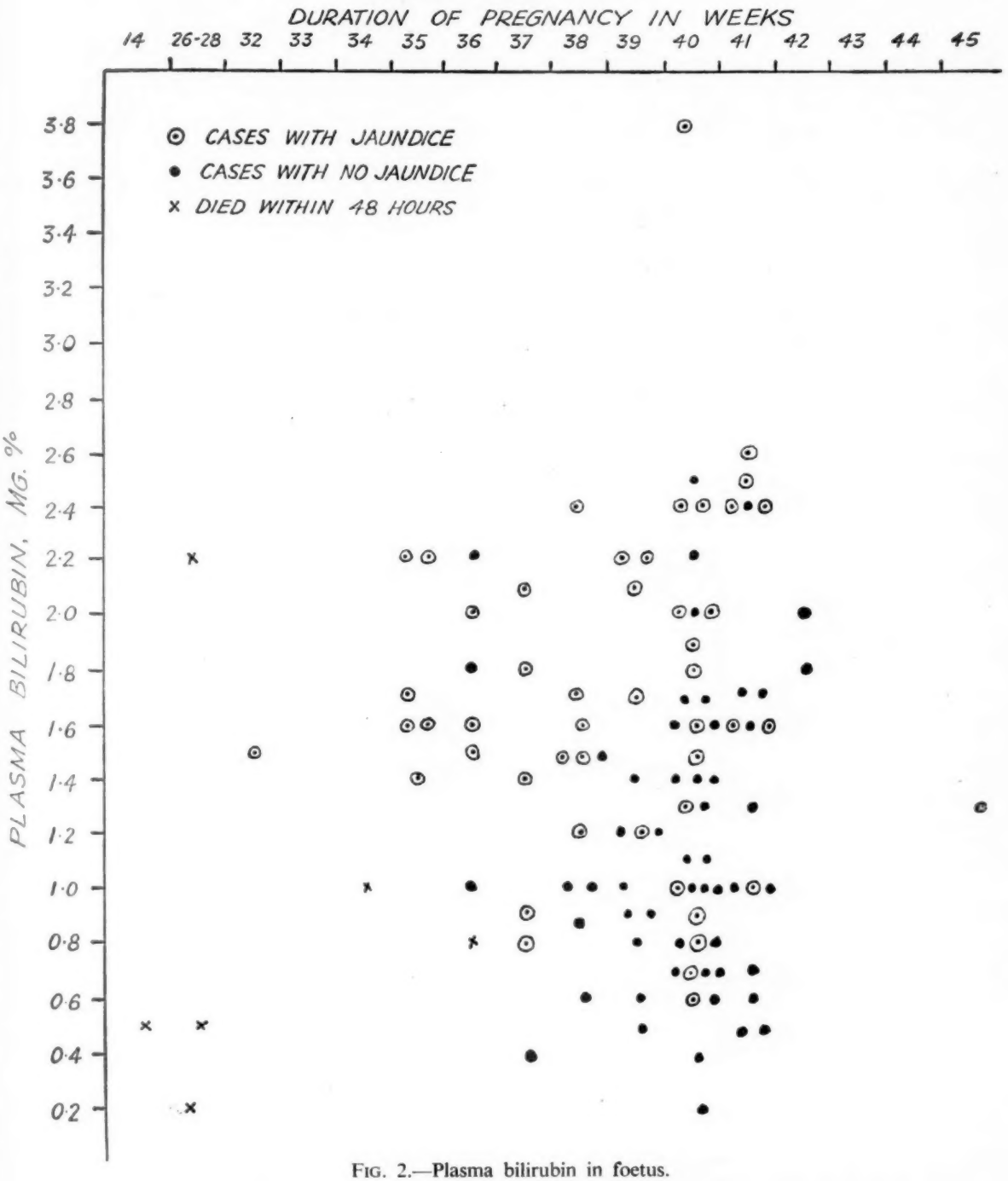

FIG. 2.—Plasma bilirubin in foetus.

These graphs bear out the finding that there is no absolute correlation between the foetal level and the post-natal rise of the plasma bilirubin. The plasma bilirubin of cord blood in group A was on the whole higher than in group B, but only slightly and not invariably. Of the whole series, hyperbilirubinaemia was present at some stage during the first ten days in all except three cases, i.e. it was present in 81 per cent. of the cases.

Relation of jaundice to maturity of infant. Although our figures show no correlation between cord blood bilirubin levels and maturity of foetus, certain findings confirm the view that the premature infants are more likely to develop jaundice than

the mature ones. One hundred and ninety-six infants were examined daily and the results are recorded (table 2, p. 73). In our experience all infants born after a pregnancy of thirty-five weeks or less develop jaundice, as against 67 per cent. of those born after thirty-six or thirty-seven weeks, and 47 per cent. of full-term infants. These findings refer to jaundice; some degree of hyperbilirubinaemia is present in almost all infants but is more likely to be severe and thus to cause jaundice in the premature.

Nature of Icterus Neonatorum

In this section we propose to discuss in turn excessive haemolysis and hepatic immaturity as causes of icterus neonatorum, to report our own findings and to show their bearing on the current theories of the origin of neonatal jaundice.

Current theories of etiology of icterus neonatorum. Several factors have been suggested in the past as possible causes of icterus neonatorum. Those most frequently mentioned in the literature are excessive haemolysis or hepatic immaturity or both. Snelling (1933) suggests that the condition results from the rearrangement of the circulation at birth, together with a delay by the liver in assuming its post-natal functions. Davidson et al. (1941) and Fallon (1943) attribute it to excessive haemolysis due to release of the foetus at birth from anoxia, together with functional immaturity of the liver. Tocantins (1940) mentions only hepatic immaturity. McIntosh (1941) declares that virtually all newborn infants show a hyperbilirubinaemia in their first week of life whether or not they develop jaundice, and that the origin of the extra bilirubin is the red cells no longer needed. Lightwood (1943) considers the condition to be haemolytic in origin, but states that the depth and duration of the jaundice is determined more by the functional capacity of the liver than by the amount of blood destruction. According to Schick et al. (1942), the condition is due to the breakdown of the mother's blood in the placenta.

Excessive haemolysis. The fall in haemoglobin concentration and red-cell count which undoubtedly occurs during the early days of life has led to the assumption of an excessive haemolysis at this period of life, a condition seen in haemolytic anaemia. The fall in haemoglobin and number of red cells could, however, be explained by a deficient production rather than a removal, or by an increased amount of plasma, thus causing a dilution effect. Our results show that this fall does not run parallel with the development of jaundice.

Rate of fall of haemoglobin and red-cell concentrations. A recent study by one of us (Findlay, 1946) showed that the most rapid fall in haemoglobin level and cell count occurs not in the first week of life, when there is a tendency to jaundice, but in the second week, when the bilirubin level is returning or has returned to normal (table 3). Further, this fall continues to the third month, long after there is any tendency to jaundice. The rate of fall of haemoglobin has also been studied in the jaundiced and non-jaundiced infants, and no difference could be detected in the two groups (fig. 4).

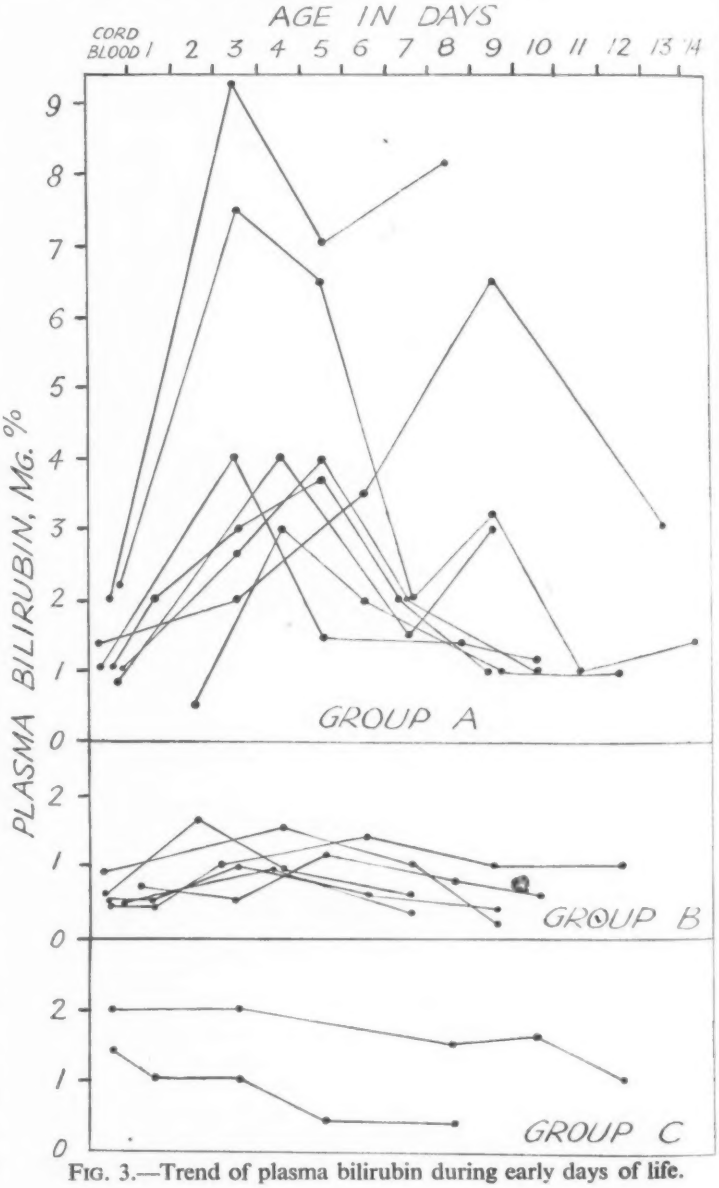

FIG. 3.—Trend of plasma bilirubin during early days of life.

Absence of concomitants of excessive haemolysis. There was also in the newborn an absence of the usual blood findings in increased haemolysis, i.e., the presence of large numbers of immature cells (reticulocytes and nucleated red cells) in the circulating blood. Except for the first few hours after birth, nucleated red cells are absent from the blood of the newborn, and the reticulocyte count is not above 1 per cent. This contrasts with foetal blood from the umbilical cord, which contains fairly numerous nucleated red cells and always has a reticulocyte count above 1 per cent.

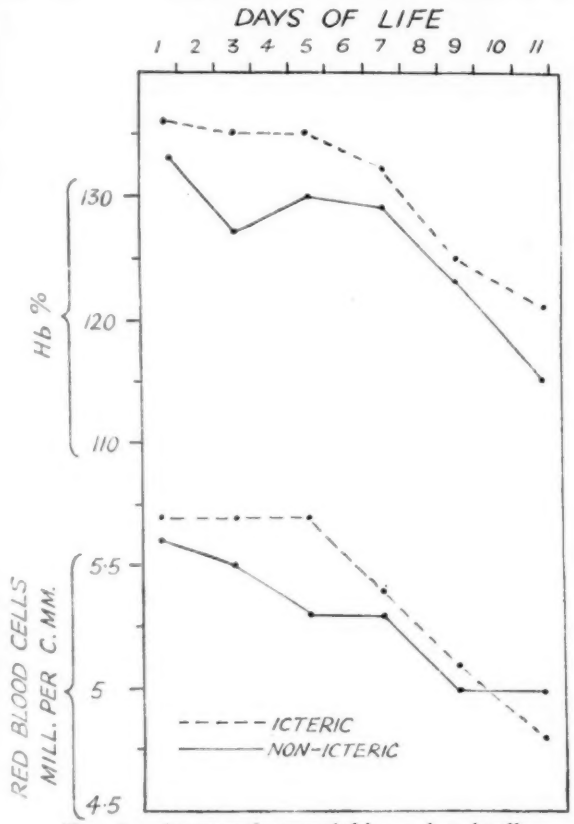

FIG. 4.—Average haemoglobin and red-cell concentrations in icteric and non-icteric infants during the first eleven days of life.

These facts suggest that a slow-down of haemopoiesis rather than increased red-cell destruction is the cause of the lowering of the haemoglobin concentration in the newborn. Considering the diminution of haemopoietic tissue which occurs in the change-over from foetal to post-natal life, it is not surprising that blood formation should slow down until extramedullary haemopoiesis is well established. It has been shown (Gilmour, 1944) that when there is a definite haemolysis, as in erythroblastosis foetalis, the extramedullary haemopoietic tissue is abnormally widespread and hyperplastic; we, however, have noticed an aplasia in the normal child.

Presence of a haemolysin. Many workers have searched for abnormal susceptibility to haemolysis of the red blood corpuscles in the newborn, or for the presence of some haemolytic agent, but the findings are conflicting. The presence of a haemolysin in the mother's serum which can affect the cord blood has been reported (Mitchell, 1928), but this could not be confirmed by other workers (Goldbloom and Gottlieb, 1929).

Fragility of red cell. The published results of the fragility of the foetal red cell in hypotonic saline are also contradictory. Some authors claim that the fragility is increased in the foetal and newborn child (Cathala and Daunay, 1908; Wollstein, 1928; Goldbloom and Gottlieb, 1929); on the other hand, Mitchell (1928), observed no difference in the red-cell fragility in early and adult life.

In a study of this question, one of us (Findlay, 1945) found a slightly increased fragility in the red cells in foetal blood and a decreased fragility during neonatal life. As far as our observations are concerned, there is no reason to assume an increased tendency to haemolysis during the period when icterus neonatorum occurs.

The effect on the foetus of the oxygen deficiency in the uterus has often been considered analogous to that of the low oxygen tension on people at high altitudes or in chambers under reduced pressures; polycythaemia present at birth has been compared with that found in residents at high altitudes. The results of experiments (Goldbloom and Gottlieb, 1930) in which guinea-pigs were placed in chambers in reduced atmospheric pressure and then removed, were very similar to the findings in people living at high altitudes and then descending to sea-level (Barcroft, 1925). However, these conditions are not analogous to life in utero, ending at birth. Although an increase in the icteric index was noticed in some animals, in several cases the increase occurred before the release from the reduced pressure, and in all cases it steadily declined on returning to normal atmospheric pressure. The raised icteric index could be explained on the basis of liver inefficiency, resulting from anoxaemia. In polycythaemia vera, in which higher red-cell counts are found than in residents at high altitudes, a raised plasma bilirubin level is most unusual except in the presence of a developing anaemia (Minot and Buckman, 1923).

Polycythaemia of reduced pressures cannot be compared with that of the newborn, or used as evidence of the haemolytic origin of icterus neonatorum. The evidence from red-cell fragility is dubious, and the evidence from red-cell counts is capable of alternative explanation. We therefore reject the theory of excessive haemolysis as the cause of icterus neonatorum.

Hepatic immaturity. If, as the foregoing evidence suggests, red-cell destruction and bilirubin formation take place in the newborn at a rate no greater, and perhaps lower, than in adults, it seems probable that the hyperbilirubinaemia is due to the failure of the

liver of the newborn child to excrete the pigment at the normal adult rate. Such a failure would not be surprising. Many tissues of the body do not reach their full powers until some time after birth. So, too, it may be expected that the premature child will be more likely to show a severe degree of hyperbilirubinaemia than the full-term child, just as the premature infant shows great variations in body temperature because of the incomplete development of the nervous system. If the curves of plasma bilirubin levels for the first ten days of life are grouped according to the duration of pregnancy, the relationship of post-natal rise to maturity can clearly be seen (fig. 5). In general, the longer the pregnancy, the less the rise.

It is only after birth that the liver starts to take on many of its functions. During foetal life, most of the portal blood is by-passed to the placenta, the liver being mainly a haemopoietic organ. Meconium contains bile pigment, so a small amount of pigment must be excreted by the liver; but probably a large proportion of the bilirubin formed in the foetus is transferred through the placenta to the mother's circulation.

Certain writers (e.g., Ylppö, 1913) have denied that foetal bilirubin is normally excreted via the placenta, on the ground that the mother's plasma bilirubin level is not raised during pregnancy. However, the daily amount of foetal bilirubin would be only a small fraction of the amount produced by the mother herself and could not cause a noticeable change in the maternal blood. Furthermore, there is positive evidence that the placenta acts as an excretory organ for foetal bilirubin. In seven newborn children the bilirubin level in the umbilical artery was higher than in the umbilical vein, the average difference being 20 per cent. (Cserna and Liebmann, 1923). We have confirmed this observation (table 4). We did not obtain the consistent results reported by the previous workers; the average bilirubin level, however, was 14 per cent. higher in the arterial blood than in the venous blood.

There is reason, to think, then, that at birth the route of bilirubin excretion changes suddenly from the placenta to the child's own liver; and if the child's liver were functionally immature at birth a temporary accumulation of bilirubin in the blood could readily be explained.

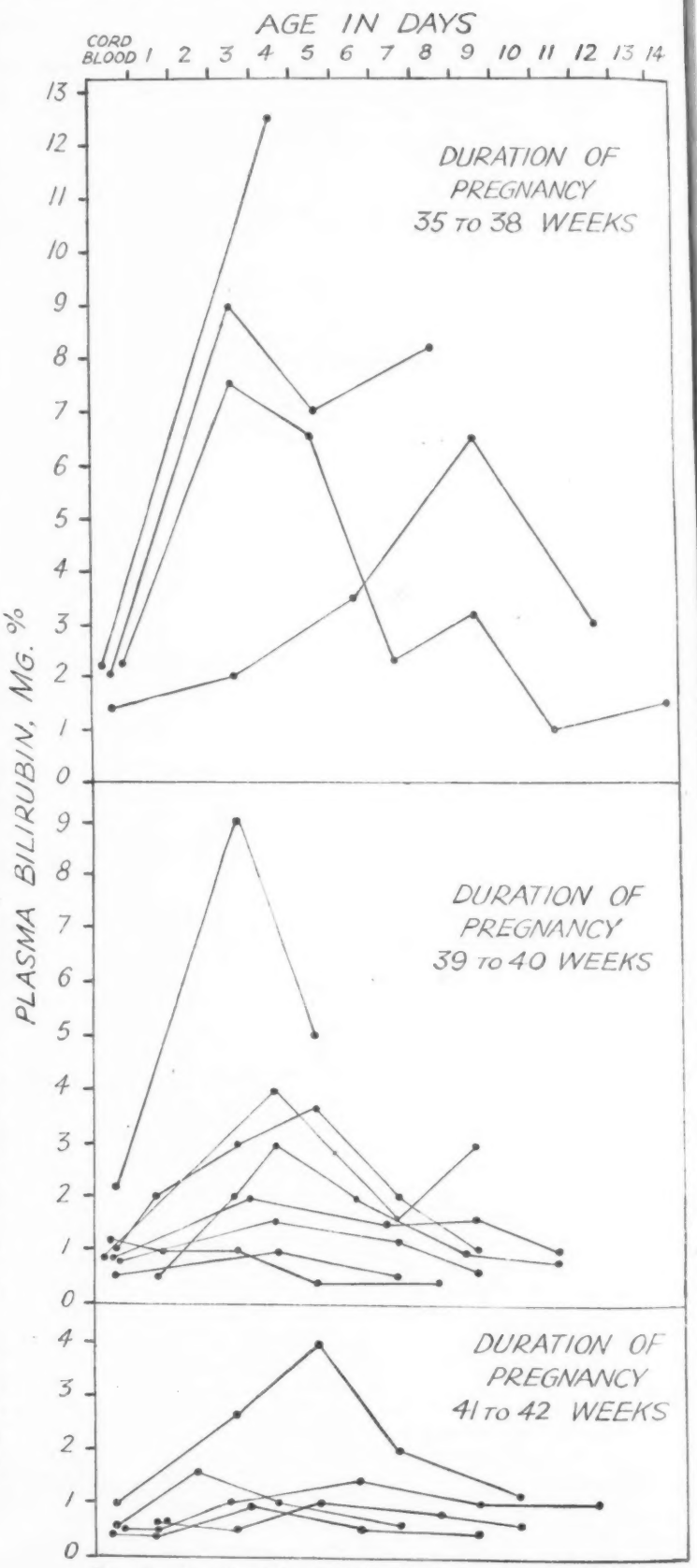

FIG. 5.—Trend of plasma bilirubin in early days of life according to degree of maturity of child.

Despite the practical difficulties, some attempts have been made to measure the efficiency of hepatic function in newborn infants. The results, however, have not been decisive. Heynemann (1915) tried to evaluate hepatic function in 109 male infants, using as a test the urinary excretion of laevulose after a standard dose. He concluded that there was evidence of impaired function of the liver in newborn babies, more marked in jaundiced than in non-jaundiced infants. Recent criticisms of this test, and also of the bromosulphophthalein test used by Herlitz (1926), however, render these results of doubtful value. Linzenmeier and Lilienthal (1922) used the post-prandial leucocyte reaction as a test, and, although they found the leucopenia after a breast feed more marked in the jaundiced than in the non-jaundiced child, other workers (Hainiss and Heller, 1923; Simon and Wellewa, 1924; Joseph and Guskar, 1924) were unable to confirm this. Ross et al. (1937) have reported an increased bilirubin and urobilin excretion in non-jaundiced infants as compared with jaundiced infants, and Waugh et al. (1940) have shown that the rise in plasma bilirubin in icterus neonatorum is confined to an increase in the indirect reacting type of bilirubin only.

We have investigated the state of hepatic function by a study of the plasma proteins and Takata-Ara reactions during the first ten days of life and of the excretion of faecal bilirubin during the first five days of life.

Plasma proteins. The total plasma proteins and albumin fraction were estimated in order to see if the changes in the protein fractions which are commonly seen in liver disease (Higgins et al., 1944), i.e., a lowered albumin and a raised globulin fraction, are observed in infants. Typical examples of our results are recorded in table 5 (p. 74). It will be seen that the results do not show any consistent changes in the albumin levels; in some cases it rose, and in others it fell. The two patients M1 and M2 were twins, and, although the jaundice in both was severe, in the less jaundiced child the plasma albumin level fell, while in the more jaundiced child it rose. Nor was any difference between the jaundiced and non-jaundiced infants observed.

The Takata-Ara reaction has been the subject of much discussion since its introduction (Takata and Ara, 1925) and opinions of its value vary considerably. Despite its limitations, the test has been used because it could be performed upon the small amounts of plasma obtainable from the newborn infants and because it is an indication of disturbed protein metabolism, since a positive test is associated with a lowered albumin and a raised globulin fraction. In so far as these are features of liver disease, this test can be regarded as an index of hepatic impairment (Higgins and O'Brien, 1947). Our results are summarized in table 6 and are not conclusive. Of the infants born after a pregnancy of forty weeks, 75 per cent. of those not developing jaundice showed a positive reaction, while of those who did develop jaundice only 66 per cent. had a positive reaction. It would appear, therefore, that there was no significant difference between the two groups. The number of tests made on infants born after a pregnancy of shorter duration was too small for any reliable opinion to be formed.

Of the twenty infants on whom we were able to do Takata-Ara reactions on both foetal and infant blood, the results were identical in twelve. In four the cord blood was positive, and in the other four the infant's blood was positive. In eight instances the mother's blood was examined during the first two days of the puerperium, and all gave a negative reaction. The changes in the plasma bilirubin and Takata-Ara reactions during the first ten days of life are recorded (fig. 6). It will be seen that there

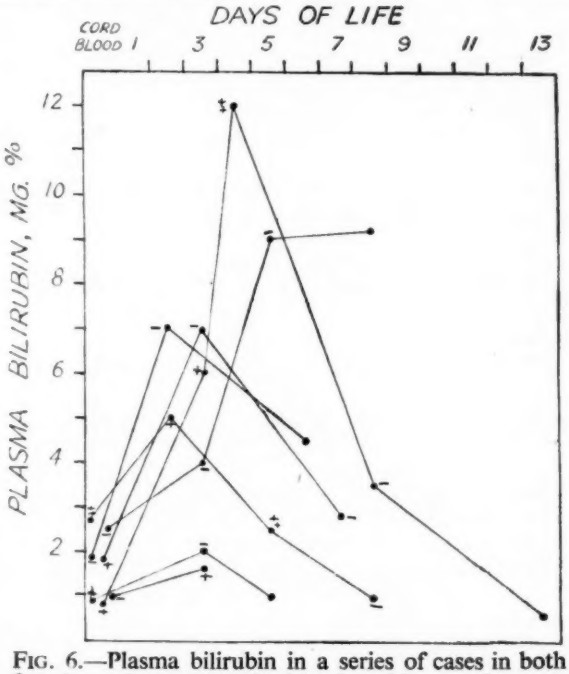

FIG. 6.—Plasma bilirubin in a series of cases in both foetal and post-natal blood with synchronous estimations of Takata-Ara reaction indicated by + (positive) and – (negative) signs.

is no correlation between the changes in the plasma proteins, as measured by the Takata-Ara reaction, and the degree of bilirubinaemia.

It is evident that the changes in the plasma proteins do not reflect the ability of the liver to excrete bilirubin.

Faecal bilirubin. It is only natural in the study of icterus neonatorum that attention should be directed to the amount of bilirubinoid pigments excreted in the faeces, since this, in the absence of an extrahepatic obstruction, should be the best measure of the amount of bilirubin passing through the liver cells. In haemolytic anaemia the amounts excreted are increased, whilst in obstructive jaundice the amounts are often much reduced. Hess (1912), using a duodenal catheter, observed the rate and

amount of bile entering the gut in the infant from a few hours after birth to the age of twelve days, and reported very little bile excreted during the first twelve hours and varying amounts during the succeeding twenty-four hours, being profuse when jaundice was marked and scanty or absent when there was no jaundice. His conclusion that there was a defective correlation between excretion and secretion is doubtful in the light of modern knowledge. He records, however, the interesting observation that when jaundice manifests itself it precedes the excretion of bile into the duodenum. Ylppö (1913), in his comprehensive treatise on icterus neonatorum, reported that he found no difference in the total amount of bile pigment excreted in jaundiced and non-jaundiced infants and that the amount bore no relationship to the intensity of the jaundice. A scrutiny of his protocols, however, shows that the average amount of bile excreted in the faeces during the first five days of life does bear a relationship to the presence and degree of jaundice, being lower in the jaundiced cases (table 7). Although some of his arguments cannot be now accepted, Ylppö was one of the first to suggest that the underlying cause of icterus neonatorum was hepatic immaturity. Ross et al. (1937) found that the amounts of faecal bilirubin and urobilin excreted by the non-jaundiced infant were greater than the amounts excreted by the jaundiced infants.

We have made observations on the faecal bilirubin excretion during the first few days of life of jaundiced and non-jaundiced children. Like the previous workers, we did not get a sharp distinction between the amounts excreted by the two groups, great variations in output being present from day to day. This was probably due to the irregularity of the faecal output. Previous workers have expressed their findings in mg. per day or mg. per cent. of faecal weight. It seems to us, however, that the amount of bilirubin formed will depend upon the total blood volume of the infant, and will thus be related to the weight of the infant. It is not to be expected that a child weighing 5 lb. would excrete the same amount of bile pigment as a child weighing 10 lb. Our results, therefore, are expressed in arbitrary units per kg. body weight (table 8). It will be seen that, even when expressed in this way, the results do not reveal a sharp distinction between the jaundiced and non-jaundiced infant, and show great daily variations. The average daily figures, and the average total for the first five days, however, show the tendency to earlier and greater excretion in the non-jaundiced infants with the lowest and slowest excretion in the severely jaundiced ones.

The excretion of faecal urobilin was also studied, but the amounts of faeces obtained preclude accurate quantitative studies. Qualitative tests showed that little urobilin was excreted in the first few days, but it was not possible to detect any difference between the groups.

Discussion

Jaundice (other than the group of obstructive types, to which icterus neonatorum certainly does not belong) may be caused by at least two factors, either singly or in combination; namely, (1) excessive haemolysis in which the amount of bilirubin formed by the breakdown of haemoglobin is too great for the normal liver to excrete, and (2) hepatic insufficiency where for some reason the liver is unable to excrete the amounts of bilirubin normally formed.

Since icterus neonatorum appears during the first week of life, the excessive haemolysis, if it be the cause, must also occur in the first week. The haematological studies, however, show that not only is the rate of decrease of the red corpuscles and haemoglobin greater in the second week when the jaundice is decreasing than it is in the first week when the jaundice is increasing, but also that there is no difference in the rates of fall in the jaundiced and non-jaundiced children. It would appear, therefore, that excessive haemolysis is not the cause of icterus neonatorum.

The question of liver insufficiency is not so easily solved; the presence of some degree of hyperbilirubinaemia in so many infants may suggest a hepatic defect, but it does not explain the occurrence of jaundice in only a proportion of those children. Tests of hepatic function, such as laevulose and sucrose tests, hippuric acid tests, and dye retention tests, cannot be applied to the newborn, and indirect tests, such as plasma protein studies, do not aid the solution. Interest, therefore, becomes centred upon studies of faecal bilirubinoid pigments. The data presented in this study support the conclusions of the other workers that, while there are considerable daily variations in the amounts of bilirubin excreted, there is a diminished excretion of bilirubin by the jaundiced infant as compared with the non-jaundiced infant in the first few days of life. It would appear then that the liver of the newborn varies considerably in its ability to excrete bile, and that in some infants it takes longer to reach an adequate efficiency than in others. This is in keeping with the facts known of other organs of the newborn. The main factor underlying the appearance of icterus neonatorum seems to be a variable liver function which quickly reaches sufficiency.

Conclusions

1. The incidence of icterus neonatorum, as judged by hyperbilirubinaemia of the cord blood or post-natal blood, is 81 per cent. There is a greater chance of a severe and prolonged hyperbilirubinaemia in a premature than in a mature infant.

2. On the basis of haematological findings, the view that the condition results from excessive haemolysis in early post-natal life is rejected.

3. Evidence derived from studies of the plasma proteins and Takata-Ara reactions is not conclusive.

4. Faecal bilirubin studies support the view that icterus neonatorum is due to hepatic immaturity.

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TABLE 1
RELATION OF FOETAL BILIRUBIN TO POST-NATAL JAUNDICE

Plasma bilirubin level in cord blood (mg. per cent).	No. of patients	No. developing jaundice	No. developing jaundice, of total per cent.
1·5	46	30	65
1·2 to 1·5 ..	22	10	45
0·6 to 1·0 ..	33	6	18
Under 0·5 ..	9	0	0

TABLE 2
JAUNDICE IN INFANTS OF VARYING MATURITY

Pregnancy weeks	No. of infants observed	No. developing jaundice	No. developing jaundice, per cent. of total
32 to 35	4	4	100
36 and 37	20	13	65
38 and 39	42	20	47
40	90	43	47
41 and 42	40	21	52

TABLE 3
DAILY FALL IN HAEMOGLOBIN AND RED CELLS IN FIRST AND SECOND WEEKS OF LIFE

% fall in	First week	Second week
Haemoglobin ..	0·4	3·3
Red cells ..	0·5	2·0

TABLE 4
BILIRUBIN LEVELS IN UMBILICAL ARTERY AND VEIN (IN MG. PER CENT.)

Artery	Vein
3·8	3·0
1·3	1·0
1·0	0·9
1·3	1·5
0·7	0·7
1·6	1·6
2·4	2·0
1·7	1·5
1·0	1·0
0·6	0·6
1·8	1·5
1·2	0·4
1·0	1·0
0·6	0·6
0·4	1·6
2·2	1·8
1·6	1·4
1·1	1·1
0·8	0·4
1·6	1·4
2·0	2·0
2·4	2·4
2·4	2·4
Average	
1·5	1·3
Difference 14%	

TABLE 5

PLASMA BILIRUBIN AND PLASMA PROTEIN LEVELS IN JAUNDICED AND NON-JAUNDICED INFANTS. (M1 AND M2 ARE TWINS.) PLASMA BILIRUBIN IN MG. PER CENT. PLASMA PROTEINS IN GRAMS PER CENT.

Jaundiced Infants

Patient	N			B			M1			M2		
Age	Plasma bili-rubin	Total pro-tein	Albu-min	Plasma bili-rubin	Total pro-tein	Albu-min	Plasma bili-rubin	Total pro-tein	Albu-min	Plasma bili-rubin	Total pro-tein	Albu-min
1 day ..	1·0	5·7	3·7	2·5	6·4	4·2	0·8	4·6	2·7	0·8	4·5	2·7
3 or 4 days ..	6·0	6·0	4·0	7·0	6·8	3·5						
6 days ..							17·5	4·1	2·0	20·0	4·7	3·0
7 or 8 days ..	1·5	5·6	3·5	1·0	6·4	4·0						

Non-jaundiced Infants

Patient	T			H			M			Th		
1 day ..	0·6	6·0	4·2	1·0	5·6	3·4	1·8	5·9	4·0	0·5	6·1	3·9
3 or 4 days ..	1·0	5·9	4·3	1·2	5·5	3·7	1·6	5·6	3·8	1·0	6·4	4·3
7 or 8 days ..	0·6	6·2	4·1	1·0	6·1	4·0		5·8	3·8	1·3		

TABLE 6

TAKATA-ARA REACTIONS IN JAUNDICED AND NON-JAUNDICED INFANTS

Duration of pregnancy	Total No. of patients	Jaundiced infants		Non-jaundiced infants	
		No. of patients	No. of patients with positive Takata-Ara reactions	No. of patients	No. of patients with positive Takata-Ara reactions
35-37 weeks ..	9	6	4 (66%)	3	0
38-39 weeks ..	4	4	3 (75%)	0	0
40 weeks ..	27	15	10 (66%)	12	9 (75%)
40+ weeks ..	6	1	1 (100%)	5	1 (20%)

TABLE 7

BILE CONTENT OF FAECES DURING FIRST FIVE DAYS OF LIFE (IN MG.) (FROM YLPPÖ)

No jaundice	Moderate jaundice	Marked jaundice
28·16 (case 1)	37·79 (case 3)	8·28 (case 2)
43·89 (case 5)	21·13 (case 4)	21·7 (case 8)
32·77 (case 7)	29·95 (case 6)	28·84 (case 10)
	33·85 (case 9)	
Average 34·9	31·0	19·6

TABLE 8

AVERAGE FAECAL BILIRUBIN EXCRETION (IN ARBITRARY UNITS PER KG. OF BODY WEIGHT)

Days of life	No. of patients	1	2	3	4	5	Total in first five days of life
Non-jaundiced ..	7	9	45	63	19	7	143
Moderately jaundiced ..	7	3	24	35	20	34	116
Severely jaundiced ..	2	0	7·5	11·5	61	12	92

A REVIEW OF 112 CASES OF CONGENITAL HYPERTROPHIC PYLORIC STENOSIS*

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Congenital Pyloric Stenosis

Congenital hypertrophic pyloric stenosis is one of the common diseases encountered during the first few weeks of life. When a survey of the literature is made, the wide variation of mortality rate reported both with medical and surgical treatment is striking. An attempt has been made to discover the factors which determined the success or failure of the treatment adopted; from records of various observers, it appeared that one of the main causes of failure was inadequate attention to the details of treatment. During a two-and-a-half-year period, a study was made of forty cases (Series A) of congenital pyloric stenosis treated in the wards and out-patient department of the Leicester Royal Infirmary, a hospital at which a detailed routine method of treatment has been employed for the past ten years. After a period of time varying from one year to two and a half years the cases were reviewed with particular reference to any physical or mental defects which could be attributed to this disease. For this purpose the children were readmitted to hospital for a detailed clinical examination and for a radiological examination of the stomach. A further series of seventy-two cases (Series B) of congenital pyloric stenosis covering an eight-year period (1938 to 1945) were also followed up clinically. Some of these had a radiological examination of the stomach.

From a study of these 112 cases, certain conclusions as to treatment are drawn and some interesting results of the radiological follow-up are recorded.

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Clinical Material

The clinical material consisted of 112 cases treated in the wards and out-patient department of a provincial general hospital serving a population of some 550,000 people. Details of the yearly incidence, etc., are found in table 1. Every case reported was diagnosed as a case of congenital stenosis on the following evidence: (a) history of projectile vomiting, constipation and, usually, loss of weight; (b) visible gastric peristalsis; (c) palpable pyloric tumour. Confirmatory evidence in the form of barium x-ray examination was only undertaken in the year 1938 (eight cases); in the remaining 104 cases the presence of a palpable pyloric tumour was taken as positive evidence of the disease without x-ray confirmation.

The average age of onset of symptoms was twenty-six days and the duration of symptoms before onset of treatment was fifteen days; thus at the beginning of treatment the average age was forty-one days. The average weight when treatment

TABLE 1

YEARLY INCIDENCE OF CONGENITAL PYLORIC STENOSIS TREATED IN THE WARDS AND OUT-PATIENT DEPARTMENT OF A PROVINCIAL GENERAL HOSPITAL

	1938	1939	1940	1941	1942	1943	1944	1945
Total new out-patients	19,458	19,288	20,578	24,739	26,394	29,093	20,532	21,782
Total children's out-patients	386	392	456	514	512	542	533	558
Total in-patients	9,676	9,372	9,794	11,571	11,962	12,141	13,178	14,028
Total children's in-patients	407	431	473	482	484	532	513	615
Cases of pyloric stenosis	8	9	11	10	18	16	21	19
Deaths from pyloric stenosis	0	0	2	2	2	0	2	4
Barium meals follow-up	3	4	2	2	9	16	10	0

TABLE 2

SERIES A: CASES GROUPED ACCORDING TO DURATION OF STAY IN HOSPITAL

	Case	Sex	Place in family	Days in hospital	Age at onset (weeks)	Age on admission in weeks	Duration in weeks	Change from birth weight ±oz.	Dose of eumydrin in c.cm.	Duration of eumydrin in days	Gain in oz. weight on discharge
Group A: in hospital ten days or less	10	M	2 (1st boy)	2	5	7	2	−16	3	28	2
	10	F	1	9	3	4	1	− 5	3	34	3
	14	M	1	6	6	8	2	− 3	3	42	9
	22	M	3 (1st boy)	8	4	8	4	− 6	3	23	5
	24	F	2	10	2	4	2	−31	3	13	7
	Average in five cases			7	4	6·2	2·2	−12·2	3	28	5·2
Group B: in hospital eleven to twenty days	6	M	5 (4th boy)	19	2	3	1	−12	5	18	14
	13	M	1	15	6	6	2 days	−19	3	42	3
	15	F	4	19	1	3	2	− 2	3	21	21
	18	M	4	14	5	6	1	− 5	3	28	9½
	21	F	1 (twin)	12	4	5	1	+ 8	1	12	9
	23	F	1	14	4	5	1	+ 1½	3–4	26	15
	26	M	2	11	2	3	1	−14	3	18	7½
	27	M	1	12	5	9	4	+ 8	Trascentin	11	18
	29	M	5	20	1	6	5	−11	4	18	11½
	Average in nine cases			15	3·3	5·1	1·8	− 5·1	3	22	12
Group C: in hospital twenty-one to thirty days	1	M	3	26	3	4	1	+10	3–5	17	15
	4	M	1	24	2	4	2	−20	3	22	12
	5	M	1	27	2	3	1	−12	3–5	8	4 R
	8	M	1	25	2	3	1	−13	3	29	21
	9	M	1	25	6	7	1	+22	3	16	9
	12	M	1	22	3	3	3 days	−12	3–5	21	10
	16	M	1	29	4	5	1	−26	3–5	35	16
	19	M	1	29	2	2	2 days	− 9	3–5–8	10	12 R
	Average in eight cases			26	3	4	1	− 7·5	3·5	20	12
Group D: in hospital over thirty days	2	M	1	40	4	4	1 day	− 4	3–5	36	15
	3	M	1	38	2	3	1	−43	5	28	21
	7	M	1	48	4	6	2	+12	3–5	46	20
	25	M	5	38	2	6	4	−56	3	36	15
	28	M	1	36	2	3	1	−13	3–5	50	11
	30	M	1	30	5	7	2	−24	3–4–5	80	33
	Average in six cases			38	3·1	4·8	1·7	−21	4	46	19

TABLE 2 (continued)

	Case	Sex	Place in family	Age at onset (weeks)	Age at first visit (weeks)	Duration in weeks	Change from birth weight ±oz.	Dose of eumydrin in c.cm.	Duration eumydrin in weeks	Gain in oz. weight on discharge
Group E: out-patient treatment	31	F	1	6	10	4	+16	3	4	56
	32	F	1	6	8	2	+25	5–7	8	64
	33	F	2	8	11	3	−26	3	4	26
	34	M	1	4	5	1	+ 8	3	3	24
	35	M	1	1	6	5	+32	3	5	64
	36	M	3	1	3	2	− 2	3	6	64
	37	M	1	6	8	2	+36	3	4	30
	38	M	3	3	12	9	+ 2	3	5	54
	39	M	2	5	7	2	+12½	3	5	38
	40	M	1	2	12	10	+62	3	5	60
	Average in ten cases			4·2	8·2	4	+16·5	3	4·9	48

was begun was 7 lb. and the average gain in weight was 4½ oz. per week.

Routine treatment. The mothers of breast-fed babies came into hospital with them and were responsible for the feeding under the supervision of the sister of the ward. The routine food for artificially-fed babies was half-cream Cow and Gate. The volume and strength of the feeds were the same as for normal babies. Feeds were given three-hourly, and eumydrin, 1 in 10,000 aqueous solution, was given half an hour before each feed. The initial dose was 3 c.cm. (0·3 mg.) and this was increased to 4, 5, or 6 c.cm. if vomiting continued. In dehydrated babies subcutaneous salines were given until dehydration was relieved, and then eumydrin was begun. The solution used for subcutaneous injection was 4 per cent. glucose in 0·18 normal saline, 50 c.cm. being given into each axilla or groin twice daily and once at night. It was found that the fluid had absorbed within three hours, and, by using the groins and axillae alternately, these sites of injection could be used until the dehydration was relieved. No skin sepsis and no persistence of oedema was encountered. The needles used were 8/10 mm. bore with record ends attached to a 20 c.cm. syringe. Ether was used for skin cleansing, wool and collodion were used locally after the injection was completed, and the area was treated as a surgical dressing.

Stomach washouts were given twice daily until there was no gastric residue. A number 5 Jaques catheter with tube and funnel attached was used through the mouth, and a funnel-full of fluid (2½ oz.) was given at a time until about 2 pints had been used to wash out the stomach. The solution consisted of 2 oz. normal saline in 2 pints of water. The average duration of stomach washouts was seven days. If severe constipation was present, rectal washouts were given about every third day until the bowels acted more regularly. If vomiting had been excessive before admission, ammonium chloride (2 gr. three times a day) was given to combat the alkalosis.

Every case was treated in a single cubicle so that cross infection was cut down to a minimum.

SERIES A. Thirty-eight of the forty cases were treated with eumydrin or other antispasmodic, and the remaining two cases (numbers 5 and 19) were subjected to Rammstedt's operation after a trial of eumydrin. Two cases (numbers 17 and 20) died while under treatment, number 17 being moribund on admission and dying within forty-eight hours, and number 20 dying of gastro-enteritis within twenty-four hours of readmission to hospital after having been previously treated successfully. Cases 15 and 26 were readmitted to hospital about two months after the pyloric stenosis had been cured, case 15 dying of a rapidly-growing retro-peritoneal sarcoma, and case 26 from a right-sided pneumococcal empyema and left pneumothorax.

Thus, of these forty cases, thirty-six responded to eumydrin, two responded to Rammstedt's operation after eumydrin had failed to relieve the symptoms, and two cases died—a mortality rate of 5 per cent. In table 2 the cases are divided into four groups depending on the duration of hospital treatment, and a fifth group consists of the cases treated entirely as out-patients. The two cases that died are not included, but are considered separately.

It has been pointed out by many observers that cases of congenital pyloric stenosis will recover spontaneously in time if death does not take place in the process. With eumydrin treatment Dobbs (1941) has emphasized that older babies respond more readily than younger ones. Mackay's (1941) series of forty cases also supports this view. The average age of onset of groups A and E of this series is four weeks, whereas in the other groups three weeks is the average time. Again in group E there was an average of 16 oz. above the birth weight

TABLE 3

SERIES B: CASES GROUPED ACCORDING TO DURATION OF STAY IN HOSPITAL

	Year	Sex	Place in family	Age at onset	Age on admission (weeks)	Duration (weeks)	Change from birth weight ±oz.	Dose of eumydrin c.cm.	Duration of eumydrin (days)	Days in hospital	Gain in weight on discharge (oz.)
Group A: Case No.											
51	1939	M	1st	6	7	1	+20	5	16	10	4
57	,,	F	2nd 1st Pyloric	2	3	1	−16	5	20	10	8
70	1941	M	1st	4	5	1	−14	5	15	5	4
82	1942	M	1st	3	5	2	+ 4	5	14	6	5
86	1944	F	1st	2	6	4	+ 5	3	5	7	2
97	1945	M	1st	4	6	2	− 2	3	21	7	4
98	,,	M	1st	4	8	4	−12	3	22	8	12
101	,,	M	1st	5	6	1	+30	3	23	9	7
102	,,	M	10th	3	11	8	−16	3	20	7	3
105	,,	M	1st	3	4	1	− 6	3	23	9	8
110	,,	M	1st (premature)	4	5	1	− 8	3	22	10	10
Average of eleven cases				3·6	6	2·4	− 1·3	3·5	18	8	6
Group B: Case No.											
45	1938	F	1st	7	8	1	−25	5	20	17	18
47	,,	F	1st	5	7	2	−12	5	14	14	18
50	1939	M	2nd 1st = girl	3	6	3	− 1	5	21	11	9
62	1940	M	1st	5	6	1	− 4	5	17	13	12
65	,,	M	2nd 1st = girl	2	9	7	−20	5	19	13	16
68	,,	M	1st	4	7	3	+ 6	5	32	25	17
74	1941	F	1st	1	2	1	− 8	3	22	18	17
75	,,	M	1st	4	5	1	−11	3	27	20	12
77	,,	M	1st	1	3	2	−26	3	24	20	7
79	1942	M	1st	2	6	4	−16	3	16	18	14
84	1944	M	1st	3	4	1	− 6	3	24	18	18
89	,,	F	3rd	6	8	2	−21	4	24	17	15
92	,,	M	2nd 1st = girl	1	2	1	− 6	Trascentin 5	Trascentin 8	20	7
93	,,	M	2nd 1st = girl	4	6	2	+ 8	3	20	15	8
94	1945	M	1st	6	7	1	+13	3	18	11	6
95	,,	M	1st	3	4	1	−14	3	18	20	20
100	,,	M	2nd 1st = boy	6	8	2	+17	3	28	20	19
108	,,	M	2nd 1st = girl	2	2	2 days	−34	3	20	12	
109	,,	M	1st	3	4	1	−13	5	18	13	9
112	,,	M	1st	4	5	1	− 3	4	20	14	15
Average of twenty cases				3·6	5·4	1·8	− 9	4	20	16	13
Group C: Case No.											
48	1938	M	1st	4	5	1	−22	5	25	28	4
49	1939	M	3rd male	8	9	1	+20	5	20	23	6
55	,,	M	1st	6	8	2	+22	5	23	25	22
67	1940	M	2nd 1st = girl	4	9	5	+ 4	5	26	29	26
73	1941	M	3rd male	1	3	2	−11	5	23	25	8
76	,,	F	1st	4	7	3	− 1	5	50	23	6
80	1942	M	1st	4	5	1	− 1	3	24	28	17
81	,,	M	1st	4	6	2	+ 7	5	28	22	18
85	1944	M	1st	3	4	1	−15	3	38	24	14
87	,,	M	4th 3 = girls	2	4	2	−15	3	25	29	18
90	,,	M	2nd 1st had pyloric stenosis	5	6	1	− 3	3	21	23	9
103	1945	M	3rd—2 girls had pyloric stenosis	4	5	1	−26	4	20	21	17
106	,,	M	1st	6	8	2	− 8	3	28	24	13
Average of thirteen cases				4·2	6	1·8	− 4	4	27	25	14

TABLE 3 (continued)

	Year	Sex	Place in family	Age at onset (weeks)	Age on admission (weeks)	Duration (weeks)	Change from birth weight ±oz.	Dose of eumydrin c.cm.	Duration of eumydrin (days)	Days in hospital	Gain in weight on discharge (oz.)
Group D: Case No.											
41	1938	M	2nd 1st=girl	5	6	1	+22	5	50	52	18
42	,,	M	2nd boy	6	11	5	+ 2	5	28	38	21
43	,,	M	1st	5	8	3	— 6	5	18	43	56
44	,,	M	2nd 1st=girl	2	3	1	— 8	6	80	90	60
46	,,	M	4th 3=girls	4	6	2	—41	5	68	79	14
52	1939	M	3rd boy	4	5	1	+ 4	8	60	62	25
53	,,	M	2nd boy	1	4	3	+ 3	5	26	46	16
54	,,	M	1st	7	9	2	+50	5	30	37	32
56	,,	M	1st	7	8	1	—30	5	29	31	35
58	1940	M	1st	2	4	2	— 6	5	36	38	17
59	,,	M	1st	1	5	4	— 8	5	35	44	22
63	,,	F	2nd girl	2	5	3	—24	5	60	67	23
64	,,	M	2nd 1st boy died after opn. for pyloric stenosis 1937	4	5	1	+ 9	5	40	43	27
66	,,	M	1st	3	4	1	—19	5	45	59	35
69	1941	M	2nd 1st boy opn. pyl. stenosis 1935	4	5	1	—21	5	36	41	31
78	,,	M	1st mother's brother died pyl. stenosis	3	4	1	— 2	5	28	34	18
91	1944	M	2nd boy	4	6	2	+11	3	18	36	7
111	1945	M	1st	3	4	1	—11	4	32	58	24
Average of eighteen cases				3·7	5·6	1·9	— 4	5	38	49	27

before treatment was begun, but in the other groups there was a loss of weight, and in group D—the six cases who were in hospital over thirty days—there was an average loss of 21 oz. below the birth weight. Nevertheless these cases did respond to eumydrin, although more slowly.

The two cases who were operated upon were in group C, and the age of onset of symptoms was two weeks; there was a loss of weight of 12 and 9 oz. respectively, and after eight days' trial of eumydrin it was obvious that operative treatment was necessary. This was in no way prejudicial to their ultimate recovery and does not support the contention that there is an added risk in attempting medical treatment before undertaking surgical interference.

Trascentin suppositories were used in cases 27 and 29 in this series, but were not as effective as eumydrin. It was hoped that trascentin would have a longer action than eumydrin thus requiring only two doses a day. In case 27, two suppositories a day for eleven days sufficed to cure the condition, but in case 29, owing to inadequate response to trascentin, eumydrin was substituted.

SERIES B. This series comprises seventy-two cases treated over a period of eight years. All the cases were treated with eumydrin, and three cases (numbers 83, 92, and 104) were subjected to Rammstedt's operation after eumydrin had proved ineffective. Two of these three cases died and are discussed later. Case 92, which survived the operation, had a pre-operative trial of eumydrin for seven days. Ten of the seventy-two cases died, and the factors contributing to this fatal outcome are discussed in a later section. The remaining sixty-two cases have been classified into four groups, depending on the length of stay in hospital (table 3).

From this table it can be seen that eighteen out of sixty-two cases, i.e. nearly 30 per cent., were detained in hospital for over thirty days. This long stay in hospital is, from the medical, economic, and social standpoints, undesirable. The causes for this long stay in hospital were as follows: six because of infections, six because of poor home conditions, and six because of slow response to eumydrin; two of these would probably have benefited from surgery.

DEATHS. Out of 112 cases, a total of twelve died while under treatment. The deaths are considered separately because it is felt that an analysis of the causes of death might throw some light on the methods for avoiding a fatal outcome in this disease. Table 4 gives in concise form the relevant facts with regard to the twelve deaths.

The most striking feature in all the cases was the

TABLE 4

ANALYSIS OF THE TWELVE DEATHS

Deaths	Year	Sex	Place in family	Age at onset (weeks)	Age on admission (weeks)	Duration (weeks)	Birth weight	Weight on admission	Hydration + / + + / + + + / + + + +	Dose of eumydrin (c.cm.)	Duration of eumydrin (days)
Case No.							lb. oz.	lb. oz.			
60	1940	M	1st	3	9	6	5 12	5 0	+ + + +	5	11
61	1940	M	2nd, 1st girl	2	3	1	6 6	6 0	+ + + +	5	14
71	1941	M	1st	4	5	1	7 12	7 7	+ + + +	5	22
72	1941	M	1st	2	4	2	9 12	6 10	+ + +	5	33
17	1942	M	2nd	1	7	6	5 3	4 12	+ + + +	5	2
20	1942	M	1st	7	12	5	5 14	7 3	+ + + +	5	21
83	1944	F	2nd, 1st girl	2	3	1	7 0	5 7	+ + +	4	9
88	1944	M	1st	3	7	4	6 0	5 0	+ + + +	3	2
96	1945	M	1st	4	5	1	6 4	6 2	+ + +	5	24
99	1945	M	1st	4	6	2	3 12	4 12	+ + +	3	10
104	1945	M	1st	4	6	2	5 8	6 5	+ + +	5	16
107	1945	M	2nd, 1st girl	4	6	2	6 0	7 14	+ +	5	10

degree of dehydration which was present when they were admitted to hospital. Six out of twelve cases were grossly dehydrated (+ + + +), and five of the remaining six cases were severely dehydrated (+ + +). An infective cause for the dehydration was present on admission in only two cases (cases 96 and 107), and was present in case 20 on the second admission after being treated initially with success by eumydrin. Case 88 was a twin, and case 99 was a seven-weeks premature baby. Thus at least ten of these cases might have been successfully treated surgically if operated upon within twenty-four hours of admission. Rammstedt's operation was performed on two cases (cases 83 and 104) on the ninth and sixteenth day respectively, but this procedure had obviously been employed after too long a delay.

Another feature of these twelve cases was the low birth weights. Nine of the twelve cases weighed less than 6½ lb. at birth, there being a wide variation from 3 lb. 12 oz. to 6 lb. 6 oz. The remaining three cases weighed 7 lb., 7 lb. 12 oz., and 9 lb. 12 oz.

Of the total 112 cases in series A and B, only eighteen weighed 6½ lb. or less at birth, and 50 per cent. of this number died.

The age of onset of symptoms, and age when treatment was commenced, showed no variation from the successfully treated cases.

One point which may have a bearing on the successful outcome of operative treatment is shown in case 83. This baby developed bronchopneumonia within twelve hours of the administration of open ether, and died two days later. Local anaesthesia might have tipped the scales in favour of a successful outcome in this case.

Discussion

A survey of the literature from 1910 to 1944 reveals that the total mortality rate both for medical and surgical treatment is the same, 11·8 per cent. in a series of 4,162 cases medically treated and 3,508 surgically treated. There is, however, a wide variation in the percentage of successful cases. For example, in 1910, Hutchison treated medically sixty-four cases, and fifty died, a mortality rate of 78 per cent.; whereas in 1930 Wolff treated ninety-eight cases medically and two died, a mortality of 2·0 per cent. Again, in 1914, Holt treated twenty-nine cases surgically, and seventeen died, a mortality rate of 58 per cent., whereas in 1941 Levi treated 100 consecutive cases surgically without a death. Such statistics probably do not reflect favourably upon either form of treatment having regard to the year in which the cases were studied, and the number of workers involved. A better gauge of the relative merits of the two forms of treatment is obtained by a study of the results of workers in the same town or institution.

In 1935 Svensgaard published her results in cases studied from 1911 to 1934, and divided them into three groups, depending on the type of medical treatment employed. From 1911 to 1927, seventy-one cases were treated by lavage and duodenal tube, and ten died, a mortality of 7·1 per cent. From 1922 to 1927, forty-seven cases were treated with atropine, and three died, a mortality of 6·4 per cent. From 1927 to 1934, sixty-one cases were treated

with eumydrin and two died, a mortality of 3·3 per cent. In 1937 there was a 10 per cent. mortality from surgical treatment at the Hospital for Sick Children, Great Ormond Street, London; in 1938 the mortality was 9 per cent., and in 1939 6·5 per cent. Thus with both methods of treatment there has been a fall in the mortality rate, probably resulting from the employment of a definite detailed routine method of treatment for this condition.

The aim of both medical and surgical treatment of pyloric stenosis is to overcome the obstruction to the outflow of food from stomach to duodenum, an obstruction which will relieve itself in time provided that the patient does not die from malnutrition in the process. Both methods aim at hastening this natural process of recovery. Wollstein (1922) has shown from post-mortem material that three or four weeks after division of the circular muscle of the pylorus (Rammstedt's operation) there is hardly any anatomical abnormality to be noted at the pyloric end of the stomach. After medical treatment with antispasmodics, a similar result is obtained, but in a longer time. In case 15 a necropsy two months after clinical cure of the stenosis showed no abnormality of the pyloric muscle.

Thus, although the aim of both medical and surgical treatment is the same, there are certain guiding principles which determine the type of treatment employed and, in addition, there are certain general principles of treatment which are common to both the medical and surgical methods.

1. All cases of pyloric stenosis should be treated in single wardlets or cubicles. This is an important measure to ensure that the chance of cross-infection is cut to a minimum. Private cases invariably do better than hospital cases, and this is largely due to the greater risk of cross-infection in hospital, even with babies nursed in single cubicles.

2. All cases should be breast fed if at all possible, because the results in breast-fed babies are far better than in those artificially fed. The excellent results obtained by Levi (1941), who operated on one hundred breast-fed babies without a death, may be quoted in support of this statement. Of the twelve deaths in the present series of 112 cases, only two were breast fed, seven were fed entirely on artificial foods, and three were fed on artificial foods after the tenth day. All observers are agreed that the mortality rate from diarrhoea and vomiting (so-called gastro-enteritis) is markedly higher in bottle-fed babies, so it is important in pyloric stenosis to encourage breast feeding because infection is so prone to occur in this condition. Several cases in this series were taken into hospital to re-establish breast feeding and not because of the severity of the pyloric stenosis, which could have been treated in the out-patient department.

In the choice of medical or surgical treatment the following three criteria are important guides.

Experience of the method. It cannot be emphasized too often that in the treatment of this condition special nursing experience is essential, and it is probably true to say that it is far more important to have a good ward sister than a good house physician. I readily agree with Paterson (1941) that it would be giving the medical profession an entirely wrong idea if it were thought that all cases of pyloric stenosis could be cured if put on a properly regulated dose of eumydrin: too much stress has been placed on the action of the drug, and too little stress on the careful nursing and feeding management. Bitter experience has shown how the response to treatment varies when a competent sister is on holiday.

Again, in surgical treatment, the experience of the surgeon is of vital importance. The surgical treatment of pyloric stenosis should be undertaken only by a surgeon experienced in this particular operative procedure.

Availability of treatment. In large towns where competent surgical assistance is available, the general bias is towards operative treatment. Provided that a careful technique is worked out in the light of experience, the results are satisfactory. In country districts where experienced surgeons may not be available, and in private practice, antispasmodic treatment will give good results. Babies living in the country can be adequately and successfully treated as out-patients attending the paediatric clinic once a week. Length of stay in hospital is an important factor, because each day brings an added risk of infection, and out-patient treatment with eumydrin overcomes this difficulty.

Special indications for each method. Various writers have formulated criteria which broadly indicate when medical or surgical treatment should or should not be employed. The most comprehensive criteria are those of Jacoby (1944 and 1946) who summarized these indications (table 5). The main points stressed are: (1) age of onset of vomiting; (2) duration of vomiting; (3) degree of dehydration; (4) presence of infection.

1. In thirty-four patients in the present series the vomiting began during the second week or earlier, and in thirty patients vomiting began after the fourth week. This leaves forty-eight of the 112 patients, i.e. 43 per cent., to which one of Jacoby's indications cannot be applied. If this criterion is applied to the cases that died—and all

TABLE 5

CRITERIA FOR MEDICAL AND SURGICAL TREATMENT, ACCORDING TO JACOBY

	Surgical treatment	Medical treatment
Indications	(a) Vomiting beginning in the second week or earlier. (b) Severe dehydration.	(a) Vomiting starting in the fourth week or later. (b) Vomiting continuous for three weeks or more, before the infant is first seen, provided it is not severely dehydrated.
Contra-indications ..	(a) Infection. (b) Diarrhoea.	(a) Severe dehydration. (b) Haematemesis.

these indications are guides to the achievement of a low mortality rate—we find that in six of the twelve deaths the vomiting began in the fourth week or later, and thus from this point of view the treatment should have been, and was, medical; in four patients vomiting began in the second week or earlier, and thus surgical treatment should have been employed.

2. In only twenty-seven cases out of 112 was the vomiting continuous for three weeks or more before the patients were first seen; and of the twelve deaths the duration of vomiting was three weeks or more in four, in four cases it was for one week only, and in four cases it lasted for two weeks. Thus again the treatment in only four of the patients who died should have been altered if this criterion of Jacoby's is to be accepted, whereas a further twenty-three cases who were cured medically should have been subjected to surgery.

3. It is difficult to know what is meant by ' severe dehydration,' but those cases requiring salines for eight days or more can be considered to be severely dehydrated. The following figures show the state of dehydration of the 112 cases as judged by the duration of subcutaneous salines:

Cases not requiring saline:	out-patients	10
,, ,, ,,	in-patients	34
Cases requiring saline for	1 to 7 days:	31
,, ,, ,,	8 to 14 ,,	23
,, ,, ,,	over 14 ,,	14

Of the twelve deaths, nine were severely dehydrated but a further twenty-eight cases, though dehydrated, recovered with medical treatment.

4. Infection of a severe degree did not occur in the cases in this series, and there were no cases heavily infected on admission. There were, however, thirteen mild cases of B. coli pyelitis, but these quickly recovered with potassium citrate and in some cases sulphonamides in addition. I agree, however, with Jacoby that in infected cases surgery is best avoided.

Having considered these criteria, we are now in a position to judge if they are of any value in deciding which cases shall receive medical, and which surgical treatment. Table 6 is a summary of Jacoby's criteria applied to these 112 cases. This summary shows that the average age of onset of vomiting varied very little in any of the groups, and certainly no sign of prognostic value is apparent from a knowledge of the time of onset of symptoms. There is an even more striking uniformity in the duration of vomiting in all groups, with the exception of group E (the out-patient cases), so that no prognostic value can be attached to this observation. The loss of weight also bore no relationship to the severity of the disease, and the amount of infection was equally distributed among all groups except group E.

The severity of dehydration was an important factor, the most severely dehydrated babies either dying or having a long stay in hospital.

Having thus analysed the factors which may determine the successful treatment of these cases of infantile pyloric stenosis, we are in a position to formulate certain criteria which will enable a decision to be taken as to which form of treatment, medical or surgical, should be employed in a particular patient with this disease.

1. Medical treatment should be the routine method of treatment for congenital pyloric stenosis in babies who are not severely dehydrated.

2. If medical treatment is ineffective after a trial of seven days, Rammstedt's operation should be undertaken without delay, provided the baby is not grossly infected.

3. Obvious infection in the baby is a contra-indication to surgical treatment.

4. Gross dehydration is an indication for surgical treatment.

5. Surgical treatment should be employed in babies whose birth weight was below 6½ lb.

Follow-up

After intervals of time varying from eleven to thirty-two months, these cases of pyloric stenosis were readmitted to hospital for one night for barium meal examination.

The details of the child's history were obtained and the following routine questions were asked: (1) diet (breast or bottle, weaning, cod-liver oil and orange juice); (2) development (first tooth, sitting up, standing, walking, talking); (3) subsequent illnesses (especially gastric symptoms, e.g. vomiting,

TABLE 6

SUMMARY OF JACOBY'S CRITERIA APPLIED TO THE 112 CASES IN THE PRESENT SERIES

Series	Group	Number of cases	Average age of onset of vomiting	Duration of vomiting before treatment	Change from birth weight	Number of infected cases	Severely dehydrated
			weeks	weeks	oz.		
A	A	5	4	2·2	−12	2	0
	B	9	3·3	1·8	− 5	2	2
	C	8	3	1·0	− 7	2	6
	D	6	3·1	1·7	−21	2	4
	E	10	4·2	4·0	+16·5	0	0
B	A	11	3·6	2·4	− 1·3	2	0
	B	20	3·6	1·8	− 9	3	2
	C	13	4·2	1·8	− 4	3	6
	D	18	3·7	1·9	− 4	6	8
Deaths		12	3·5	2·5	− 6	3	9

anorexia, abdominal pain); (4) psychological (unrest, anxiety, temperament); (5) mental organization (playing interests, etc.); (6) family (other cases of pyloric stenosis); (7) height and weight.

Series A. The child was given a full clinical examination, and in none of the cases was there any evidence of organic disease. In no case had the pyloric stenosis hindered the subsequent development of the child. Each child was given a barium meal, and the routine preparation for this was starvation for nine hours, nothing by mouth from 12 midnight until 9 a.m. when the barium was given. At 9 a.m. the child was taken to the x-ray department and given four teaspoonfuls of barium emulsion; the child was then screened and the first film taken. Four or five additional spoonfuls of barium emulsion were then swallowed, and the child taken back to the ward. At 12 noon, i.e. three hours later, the child was again taken to the x-ray department for further screening, and the final film taken. Particular notice was taken of any deformity of the pyloric region, and of any delay in emptying time. Table 7 summarizes the results of the barium meals in Series A. This table shows that in group A (those cases under ten days in hospital) all the four cases examined had no delay in emptying, no barium remaining in the stomach three hours after the commencement of the barium meal. In group B (cases in hospital from eleven to twenty days), five of the seven cases showed no delay in emptying, the remaining two cases showing only slight delay. In group C (cases in hospital twenty-one to thirty days), there was slight delay in three of the seven cases, and definite delay in three of the seven cases. In group D (cases in hospital over thirty days) there was no delay in emptying in four of the six cases. In group E (out-patient series) there was no delay in six of the ten cases, slight delay in three cases, and definite delay in one case. Thus it is seen that in groups A, B, and C, the degree of delay was roughly proportional to the length of stay in hospital; the more pronounced the delay, the longer the cases were in hospital, and, since the length of stay in hospital in most cases reflected the severity of the disease, the delay in emptying time was an indication of the severity of the pyloric stenosis.

TABLE 7

RESULTS OF BARIUM MEAL IN SERIES

Group	No. of cases	Emptying not delayed	Slight delay	Definite delay
A	4	4 (100%)	—	—
B	7	5 (71%)	2 (29%)	—
C	7	1 (14%)	3 (43%)	3 (43%)
D	6	4 (66%)	1 (17%)	1 (17%)
E	10	6 (60%)	3 (30%)	1 (10%)

Group D, at first sight, does not fit into the general pattern, but on closer investigation it was found that three of the four cases showing no delay on x-ray examination were detained in hospital longer than the severity of the symptoms required, for the following reasons. Case 2 had a very nervous mother, and an attempt was made to re-establish breast feeding in this case. The eumydrin was stopped four days before discharge, and the condition had cleared up satisfactorily and the mother educated in mothercraft before the child was allowed to leave hospital. In case 3 the home conditions were extremely poor, and it was for this reason that the child remained longer in hospital than was necessary. Eumydrin was discontinued ten days before this child was discharged. For similar reasons case 7 remained in hospital longer

than the disease process warranted. The gain in weight of 20 oz. during the last twenty-eight days of hospital treatment supports the contention.

Thus Series A shows that there is a close relationship between the severity of the pyloric stenosis and the subsequent radiological findings from one to two and a half years later.

Series B. Of the total of seventy-two cases in this series, twenty-six were seen at the follow-up examination. Of the remaining forty-six cases, ten had died of pyloric stenosis, twelve did not attend the follow-up clinic, and twenty-four were considered to be too young for a follow-up examination to be profitable. (Their ages varied from four months to twenty months.) The routine questions asked were similar to those used at the follow-up of the cases in Series A. Clinical examination did not reveal any abnormalities, and height and weight measurements were within normal limits in all cases. Table 8 summarizes the relevant results with regard to symptoms.

Nine of the twenty-six patients had symptoms referable either directly or indirectly to the abdominal tract. These nine cases were given barium meals in order to determine if there were any visible results of infantile pyloric stenosis. In addition two other cases (numbers 43 and 57) were examined radiologically. The radiological findings were as follows: (a) cases 43, 51, 55, 74, 78, and 79 showed no contraction of the pyloric area and no delay in emptying time; (b) cases 57 and 54 showed slight contraction at the pyloric antrum, but no delay in emptying time; (c) case 45 showed definite contraction of the pyloric antrum but no delay in emptying time; (d) case 64 showed a fair amount of contraction of the pyloric area with spasm, but no delay in emptying time; (e) case 68 showed definite contraction of the pyloric antrum, and emptying was slower than in a normal case, though there was no extensive delay.

TABLE 8

SUMMARY OF FOLLOW-UP FINDINGS IN SERIES B

Year	Case no.	Symptoms
1938	45	Epigastric pain after food; constipation
1939	51	Occasional vomiting, probably due to post-nasal catarrh
	54	Bowels open after each meal
	55	'Bilious attacks': vomiting, headache, temperature, and abdominal pain
1940	64	Abdominal pain and vomiting frequently
	68	'Bilious attacks': vomiting, headache, temperature, and abdominal pain
1941	74	
	78	
1942	79	

Of the five cases showing some abnormality of the barium meal, two belonged to group B (eleven to twenty days in hospital), and three belonged to group D (over thirty days in hospital). These findings tend to support the conclusions drawn from the results of barium meal examination in Series A, namely that the more severe the case of pyloric stenosis as judged by length of stay in hospital, the more there is a likelihood of permanent structural damage to the pyloric area. No definite conclusions can, however, be drawn from the small number of barium examinations carried out upon Series B, but these results tend to support the thesis advanced for Series A.

Conclusions

1. One hundred and twelve cases of congenital hypertrophic pyloric stenosis treated medically are presented. Series A comprises forty consecutive cases, with two deaths, and Series B comprises seventy-two cases treated at the same hospital over an eight-year period, with ten deaths.

2. Particular stress is laid on the observance of a definite routine, whichever method of treatment is employed.

3. The cases in Series A were followed up clinically and radiologically. Their subsequent physical and mental development was in no way affected by the pyloric stenosis, but the delay in emptying time of the stomach when seen at the follow-up examination was proportional to the severity of the condition as judged by the length of hospital treatment.

4. The cases in Series B were followed up clinically, and some were submitted to radiological examination. The results tend to confirm those of Series A.

5. The following criteria are useful in deciding which method of treatment should be employed in a particular case of congenital pyloric stenosis: (a) medical treatment should be the routine method of treatment unless the patient is grossly dehydrated; (b) surgical treatment should be undertaken if medical treatment is ineffective after a seven-day trial, unless the patient has any infection; (c)

surgical treatment is indicated in patients who are grossly dehydrated when first seen, or in whom the birth weight was below 6½ lb.; (d) surgical treatment is contra-indicated in any infected patient because of the risk of fatal ' gastro-enteritis.'

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THE DEPOSED CHILD

BY

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This article is a survey of the alleged habits of 156 children before and after the birth of a new sibling.

Material

Mothers were questioned who had two or more children of whom the youngest was less than a year old. These women were attending five welfare centres in the Metropolitan Borough of St. Pancras. From the returns of birth notifications and of first attendances it is estimated that about 80 per cent. of the mothers in this area who have a baby less than a year old attend a centre. It therefore seems reasonable to consider these mothers as representative of the district, remembering, however, that they do not include those who are rich enough to go elsewhere, or those who are too busy or too careless to attend anywhere. Most of the mothers were attending with a new baby, and not because of the ex-baby about whom questions were asked. Eighty-five per cent. of their husbands were artisans or labourers, and 15 per cent. were clerks or highly skilled technicians; 94 per cent. were British. Of the children, 102 (Group A) were under five years old, and 54 (Group B) were between five and fourteen years old.

Method

Consecutive mothers were questioned by the writer. Half of these attended his own clinic and the rest were waiting at the four other clinics. Five mothers were excluded during the survey. Two of these could not speak English, and a third had a cleft palate. Another had a deaf and dumb child. The fifth had three children of whom the middle one had died.

The name, age, and sex of the baby, the sex of the adjacent child and its age when the baby was born, and the number of siblings were noted. The mother was told the nature of the survey and she was asked whether the ex-baby had shown any signs of jealousy, and, if so, the time of onset and duration. Specific questions were asked regarding previous and present appetite, micturition and bowel habit; and if the child had ever hit the baby. As a rough guide to general behaviour she was asked if he stuttered, blinked, bit his nails, or sucked his thumb, and if, when annoyed, he hit his mother or 'kept it to himself.'

The father's profession and approximate length of military service were noted. The mother was asked how the child had been prepared for the new baby, and why, in her opinion, some children seemed jealous and others not. Any other comments of interest (e.g., behaviour of older siblings) were noted.

If the mother stated that her child had shown unmitigated pleasure at the arrival of the baby she was congratulated. Otherwise she was reassured that many children are disturbed at this time. The tone of questioning was not that of a cross-examination, and therefore no resentment was encountered by the writer or the health visitors.

Preparation

In group A (children under five years) 33 per cent. had been told that a baby was to be bought, and some of them had saved up for this purpose. To 27 per cent. nothing had been told at all; of these, three-quarters were under two years old. The explanation to 26 per cent. had been that a new child would be sent or fetched. This explanation was usually vague, but in one case a nurse, and in another a father, was mentioned as the donor. The facts had been told to 10 per cent. No word was heard of storks, gooseberry bushes, or doctors, though three parents had given analogies using dolls, an apple tree, and seeds respectively.

In group B (children over five years) buying persisted as the major simile; 20 per cent. were presumed to have guessed or known; and 8 per cent. had been told the truth by a parent. One mother said that babies came from China, and another that they were like flowers.

In group A, which is large enough for subdivision, there was no definite correlation between the words used and the subsequent behaviour of the child. One felt that it was not so much what the mothers said as the way in which they said it that mattered. It is, however, disappointing that such a large proportion of the older children are either told nothing or else a story which must puzzle any child who is not blind.

Ordinary Behaviour

Many children had inconvenient habits which were unrelated to the arrival of the new baby. These provide a group standard for later changes. Some of these habits were evenly distributed between

those children who later showed jealousy of the baby and those who did not.

Aggression. Before the birth of the baby 23 per cent. of the children in group A, and 12 per cent. in group B, were said to hit their mothers when annoyed. Some of the mothers who were never attacked thought that their children ' did not want to ' and others that they ' did not dare to ' hit them. In our dealings with children it is not easy to distinguish between these two types of meekness.

Appetite. Of group A, 13 per cent. and of group B, 7 per cent. had always eaten poorly. (The children in group B were at school for most of the day and therefore less under maternal observation.)

Stuttering. Of group A, 12 per cent. stuttered; none did so in Group B. Transient stammering is quite common in pre-school years.

Bowel habit. In group A, 7 per cent. had ' always been constipated '; 2 per cent. had avowed fear of the lavatory; and 1 per cent. had faecal incontinence following measles. In group B, 3 per cent. had chronic constipation.

Nailbiting and Nailpicking. These habits had existed for a long time in 7 per cent. of group A and 14 per cent. of group B.

Blinking. Eyelid tics existed in 6 per cent. of group A and 2 per cent. of group B.

Two habits occurred with different frequency among those children who later showed jealousy of the baby and those who did not.

Bed-wetting. At the time of enquiry 29 per cent. of group A and 4 per cent. of group B wet their beds. If those children are excluded who had recommenced enuresis after a marked period of control (i.e. those who began again after illness, the baby's arrival, or some clearly dramatic event), there remain twenty-three children who had never gained sphincter control, fourteen of these being over two and a half years of age at the time of enquiry. Nine of these latter fourteen were among the children who later showed no jealousy of the baby. Furthermore, the five children who were still enuretic after the age of four years were all among those who were ' not jealous ' of the baby when this arrived.

Thumbsucking. At the time of enquiry 19 per cent. of group A and 6 per cent. of group B were said to suck their thumbs. Excluding those who had recommenced this habit only after an illness or the baby's birth, there remain twenty-two children who had always sucked their thumbs. Fourteen of these were among the children who later showed open signs of jealousy of the baby, and only eight of the twenty-two were among those who did not.

The figures for enuresis and thumbsucking are small for subdivision, but they hint that early sphincter control, the thumbsucking habit, and a tendency to show resentment of a new sibling may be associated. The possible significance of this will be discussed at the end of the survey.

General Change in Behaviour

In a survey of this nature it is difficult to know how far to rely on the statements of a mother. A high proportion of truthful answers about enuresis, for example, may be expected if the survey is conducted with tact and a sense of humour. But the word jealousy is tinged with varying shades of significance.

' Jealousy.' In group A, 51 per cent. and in group B 28 per cent. were said to have shown signs of jealousy.

In group A, 3 per cent. and in group B, 2 per cent. had been taken to physicians because of the unpleasant change in their behaviour when the new baby came.

Some of these mothers merely realized that the child regarded the baby with mixed feelings, among which resentment was apparent. Other women chose to interpret the behaviour of the child as resentful, for they saw the toddler's jealousy more as a compliment than an inconvenience, and blew strongly on any spark of it which could be found.

' Absence ' of jealousy. In group A, 49 per cent. and in group B, 72 per cent. were described as not being jealous of the baby. In 10 per cent. of group A and 4 per cent. of group B there seemed to the writer to be doubt about this description. Two blatant examples are given.

EXAMPLE 1. Baby L. was ten weeks old. Dora, aged one year and three months, was said to have been not at all jealous. She had, however, been off her food for six weeks, constipated for two weeks, and, although previously a placid child, had now commenced to hit her mother when she was annoyed.

EXAMPLE 2. Mrs. J. was questioned when her baby was ten weeks old. Lucy, aged four years, had shown nothing but pleasure since the baby arrived. Mrs. J. was surprised at this, for Lucy had previously objected strongly if her mother took strange babies on her lap. Four weeks later Mrs. J. asked for another interview. She said that for the last fortnight Lucy had been a terror, climbing into her mother's bed at night and saying, ' I won't love baby if you scold me.' This behaviour had begun when she had been sent off to a nursery school with the remark, ' I'll be able to see to baby now without you messing about the place.'

In 39 per cent. of group A and 68 per cent. of group B the mothers gave fair reason for their statement that the child was ' not jealous ' of the baby. Examples are given because some writers have questioned whether any child would feel indifferent or predominantly glad to have a new sibling.

EXAMPLE 3. Mrs. Y.: ' I expect she's got so used to her baby cousins round the place that one more baby doesn't seem to make any difference.'

EXAMPLE 4. Mrs. P.: ' He was so jealous of my husband when he was demobbed that he is glad to have baby as something for himself to look after. Maybe he spent all his jealousy on his father.'

EXAMPLE 5. Mrs. R.: 'I've an invalid husband and there is never any time to fuss either the girl or the baby.'

EXAMPLE 6. Mrs. O'C.: 'I told Joe (aged three years nine months) that we were going to get a baby off the apple tree. He was in the room when I was in labour and he did not like that so he ran out. But he soon came back. I thought that he would be jealous, specially as it was twins and as he had been alone with me till his dad came home last year. But apart from perhaps crying a little more he has not minded a bit. . . . Of course he has always hit me occasionally. . . . But he goes out to play and when he comes in he pops over to look at the babies and is almost fatherly. I suppose it is because he is of an independent nature and because I like bringing up kids.'

Most emotions are hybrid. The purpose of this section has been to indicate in general terms how much children vary in their behaviour after a particular crisis.

Specific Changes in Habit

Aggression. In group A, 26 per cent. and in group B, 6 per cent. hit, pinched, bit, or pulled the hair of the baby. This was often a source of anxiety to the parents.

In group A, 11 per cent. who had previously been docile began to hit their mothers after the baby arrived. One child was said to have begun hitting a beloved grandmother with whom he had stayed during his brother's birth.

Appetite. In group A, 21 per cent. had anorexia after the new baby came. This usually began immediately, but was occasionally delayed until the baby was brought to the table for meals. It most often lasted a few weeks, but the variations were between three days and nine months or more. There was loss of appetite through incidental illnesses (e.g. after measles) in 4 per cent. Three per cent. ate much better after the baby arrived. In group B 7 per cent. lost their appetite when the baby was born, and 4 per cent. had eaten much better since then.

Loss of appetite in these children was almost always accompanied by other signs suggestive of resentment. On the rare occasions when this was not so, it is possible that the new baby was just a pleasant distraction, of greater interest than food. One does not know whether the children whose appetite increased were altogether more happy, or if they were merely easier during meals now that the maternal eye was fixed on the baby.

Bowel habit. In group A, 3 per cent. had been constipated for a few weeks shortly after the baby's birth. Two per cent. refused to be taken to the lavatory except during the baby's feeds, 1 per cent. had diarrhoea associated with much aggressive behaviour when the baby was a few weeks old. In group B, no change in bowel habit was reported.

Bed-wetting. In group A, 5 per cent. had recommenced enuresis or wet their beds much more frequently since the advent of the baby. One girl, aged two years nine months, said frankly that she did not see why she should not copy the baby. In group B, 2 per cent. recommenced bed-wetting after the baby was born.

Thumbsucking and nailbiting. In group A, 5 per cent. had begun thumbsucking or grossly exaggerated this habit since the baby's birth; 2 per cent. had begun nailbiting and nailpicking. In group B, 1 per cent. had adopted a finger-mouth habit when the baby came.

Blinking and stuttering. There seemed no association between the onset of these habits, when present, and the arrival of the baby.

Influence of Sex

The sex of the baby and that of the adjacent child have no influence on the early relations of the two as seen in this survey. When group A and group B are subdivided into the pairs MM, MF, FM, and FF, these arrangements are approximately the same among the 'jealous' and 'non-jealous' children.

Influence of Age

The influence of age is shown in table 1 and in the figure. The curve of increasing emotional maturity is not smooth. In this it resembles Gesell's description (1941) of the development of neuromuscular co-ordination in children. Overt jealousy has its peak of incidence in the third year, which is also notorious for difficulties in speech and in movement. It should also be noted that no child is too young or too old to behave with great inconvenience to himself and his parents if he thinks that he has been displaced. Three examples are given because of their age.

TABLE 1
INFLUENCE OF AGE

Age in years	No. jealous	No. not jealous	Group
0–1½	8	6	A
1½–2	11	10	
2–3	15	8	
3–4	10	16	
4–5	8	10	
5–6	3	9	B
6–7	3	7	
7–10	7	16	
10–14	2	7	

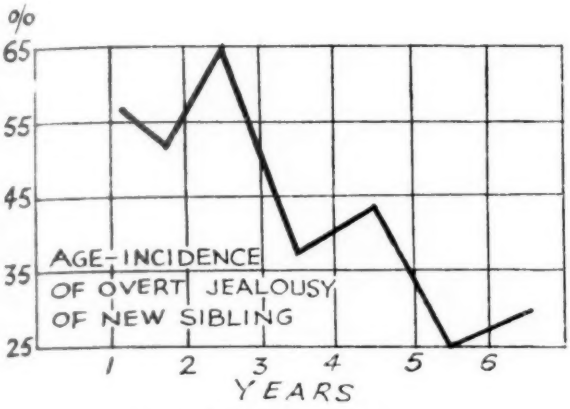

FIG. 1—Influence of age.

EXAMPLE 7. ' Roddy (aged ten months) did not like baby from the first. He is puzzled at my breast feeding, and he is always awake now (aged thirteen months) when I go in to give baby the ten o'clock feed. He asks for tea then. He hits baby and me often. When baby is taken up he hides his face in his hands.'

EXAMPLE 8. Winston, aged fifteen months when his baby brother was born, stayed with his grandmother for two weeks at that time. His mother said: ' He used to be good, but since his return he won't play with his nice toys. He waits till I begin to breast-feed baby, and then he bangs tins and bottles together. He screams at night now, and he gets terrified of things like caterpillars and the fur collar of my coat. My milk is going, he worries me so much. But he kisses baby a lot and doesn't hurt him.'

EXAMPLE 9. ' Ronald (aged fourteen years) said that if the new baby was a boy he would throw it out of the window and if it was a girl he would gas it. He has done neither but I am not happy about him and baby.'

Influence of Family Size

Table 2 shows the number of families of different sizes in the survey. This shows no evidence in support of two facile generalizations, frequently voiced, namely, that ' only ' children are specially liable to resent the advent of a new sibling; and that a large family is in itself the guarantor of a spirit of ' give and take.' The early behaviour of children would appear to depend much more on who is running the family and on the particular status of each child in the family group.

TABLE 2
INFLUENCE OF FAMILY SIZE

No. of children	Group A		Group B	
	' Jealous '	' Not jealous '	' Jealous '	' Not jealous '
2	32	30	7	22
3	10	13	7	9
4	4	4	1	3
5+	6	3	0	5

Prevention and Treatment of Jealousy

All the mothers maintained that they had foreseen the possibility of the child resenting the arrival of a new baby. But, apart from the verbal announcements noted above, most had waited to see what would happen. When the baby arrived some women instinctively treated the displaced child as Stekel (1931) and other leading psychiatrists have recommended. That is, they assured him of their continued affection and encouraged him to take an active part in the care of the baby. It should be emphasized here that the spirit behind the action is very important. One mother, who gave her toddler the dregs of the baby's bottle, had not really understood his needs.

Conclusions

To look at any child through a tracing of percentages would be a bad prelude to assessment. In this survey a map of habits and changes in habit has been sketched. Against the background of this it should be possible to keep a sense of perspective when looking at a child, and to appraise him better.

The incidence of certain inconvenient habits in ' normal ' children has been indicated. The proportion of children with chronic aberrations of appetite and bowel habit is smaller than might appear from the numbers who wait in surgeries. Conversely, there are many late enuretics, and many pre-school children with tics, stammering (Edwards, 1939), and aggressive behaviour who never reach the out-patient department.

After the new baby arrives the behaviour of the deposed child is by no means uniform. One regards the baby mainly as a plaything, of rather more interest than a puppy. Another sees the new baby as a supplanter; his mind and body are greatly disturbed, and, with the thumb of one hand in his mouth, he strikes the baby with the other, resorting to infantile habits himself. A third child, after a short period of overt jealousy, seems to decide, with his mother's encouragement, that he will be independent. He patronizes the baby and begins to grow up.

What factors influence the expression of such feelings? That of age is clearly shown in the survey. But the vast influence of previous upbringing, mingled with hereditary traits, is subtle, and only hints of it emerge in a survey of this size. A

strong clinical impression was gained that the casual though affectionate mother had the least bother with her child. That these mothers were not over-attentive, even before the new baby arrived, was suggested by the higher incidence of late sphincter control among their children (cf. Maberley, 1945). There were also fewer thumb-suckers among the ' non-jealous ' children. Now, although the significance of thumb-sucking has not been decided (Valentine, 1942), it is at least a gratifying habit to which older children resort more in times of relative loneliness (e.g. at night and with strange adults). It is possible that the bulk of the non-jealous children had been forced into self-dependence early in life and did not need the extra solace of a thumb in the mouth. In general the child of a phlegmatic mother may not be clean in his habits, but he has grown to depend on himself at an early age; and he sees little cause for anxiety when his mother nurses a new sibling.

The questionnaire method has been neglected in the study of normal children (Bühler, 1935). Its value is limited, but may be considerable in emphasizing the wide range of so-called normality.

Summary

At welfare centres in St. Pancras, London, 156 mothers of two or more children were questioned about the habits of the ex-baby. The incidence of certain inconvenient habits before and after the arrival of the new baby is noted, with special reference to those in children under the age of five years. The influence of preparation, sex, age, family-size, and previous upbringing on overt jealousy is discussed.

I wish to thank Dr. Dennis Geffen for his criticism of this paper, and the health visitors of St. Pancras for their interest in the survey.

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EMPYEMA THORACIS IN INFANTS AND CHILDREN*

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Introduction

Although empyema thoracis was known to Hippocrates, there was no real advancement in treatment until the middle of the nineteenth century. Roe (1844) introduced repeated aspiration instead of simple incision by knife or cautery when the necessitas state had been reached. Intercostal drainage was soon to supersede this method (Goodfellow and de Morgan, 1859), which in turn gave way to rib resection, accredited to various persons, including Walter (1860) and Roser (1865). With improved technique the latter method gave better results and became the standard method of treatment. A setback was experienced in the war of 1914-18, when a change in the causal bacterium occurred. An alarming death rate was responsible for the formation of the Empyema Commission (1918), whose findings still form the basis of treatment to this day. With modified methods and improved technique mortality rates were soon reduced except in children, especially during the first two years of life. This feature is revealed in the many recorded series of cases of empyema occurring in children. Brown, J. P. (1923) reviewed 250 empyemata in children. The cases were admissions in the Children's Hospital, Philadelphia, from 1906-22. A general mortality rate following rib resection was 21·5 per cent., and after intercostal drainage was 40·3 per cent. The mortality in the first year of life was appalling.

The position was discussed at a British Medical Association Conference in London, 1925. Cameron and others emphasized that the early years of life carried a grave prognosis whenever empyema was diagnosed. Of fatal cases, many were shown to have synpneumonic empyemata. Additional serious lesions were frequently present, e.g. pericarditis and mastoiditis, and this feature was found to indicate a slender chance of survival. Strong support was given to the policy of aspiration in the case of synpneumonic empyema. No surgical interference was recommended until the active pneumonic process had resolved.

Osman and Cameron (1925) reported the details of fifty-two empyemata in children, all under two years of age. No fewer than thirty-nine children died, and of the thirteen recoveries only one had a synpneumonic type of empyema. The mortality rates were: under 1 year, 66 per cent.; from 1 to 2 years, 50 per cent. Further facts were recorded by Spence, R. C. (1920). He had studied 204 cases of empyema in children under three years of age. The general mortality rate was 44·6 per cent. Sixty-four per cent. of children died in the first year, and 50 per cent. between 1 and 2 years of age. It was shown that the mortality rate decreased with increasing age. Similar findings were noted in the cases of Ladd and Cutler (1924), Farr and Levine (1928), Reinhoff and Davison (1928) and Heuer (1932).

C. R. Steinke (1935) reviewed the literature to date, and recorded 310 cases of his own. These cases were divided according to the different bacteriological groups, and the mortality figures showed that the pneumococcal cases carried the least mortality, while those due to the staphylococcus were most lethal.

Hochberg (1941) stressed the value of closed intercostal drainage in large seropurulent effusion, especially when aspiration had failed to relieve respiratory distress. He also pointed out the risk of infecting the chest wall by repeated aspiration, especially in staphylococcal cases. When reporting a series of 474 surgically treated cases of empyema, Lanman and Dimmler (1941) noted a reduced mortality with improved surgical technique. As the cases covered the period 1919-39, it is significant that they had noticed a marked reduction in the incidence of empyema since the use of sulphonamides in the treatment of pneumonia in 1938.

In the present paper cases of empyema are studied for two five-year periods, 1934-38 and 1940-44, and by comparison the effect of the sulphonamide groups of drugs upon the incidence of empyema is shown. With the relative increase in cases due

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to the staphylococcus aureus, an account of staphylococcal pneumonia and empyema is given. Since penicillin became available for general use in January, 1945, a new phase in the treatment of empyema caused by sensitive organisms has been opened. In section II of this paper the use of penicillin in staphylococcal and sulphonamide resistant pneumonia is discussed, and a collected series of twenty-one cases of empyema treated with penicillin reviewed, illustrating the improved prospects in the most critical age group, namely, in the first two years of life.

PART I

EFFECT OF SULPHONAMIDES ON THE INCIDENCE, MORTALITY RATES, AND BACTERIOLOGICAL FINDINGS IN EMPYEMA THORACIS OCCURRING IN INFANTS AND CHILDREN

The admissions of empyemata in children and infants have been studied for the period 1934-44 inclusive. These admissions (totalling 275) were to a large general hospital in the City of Birmingham, and represent all cases of post-pneumonic empyema without selection. Cases have been segregated in each year according to age, and according to the bacterial agent responsible. Mortality rates are also given. The period 1934-38 is taken as a five-year period in which sulphonamide drugs were not used in the treatment of acute pneumonia. The year 1939 is omitted, as in this year accurate details are lacking about the proportion of cases treated with and without sulphonamides. The period 1940-44 represents the five-year 'sulphonamide' period, which is compared with the 1934-38 period in order to assess the effects of sulphonamide drugs upon the incidence of empyema as a complication of acute pneumonia in children and infants.

The admissions of acute pneumonia to the hospital have been studied, and, when the same two periods are compared, it is found that the reduction in the admissions in the second five-year period is responsible only to a slight degree for the actual reduction in the numbers of empyemata. The most important factor is undoubtedly the sulphonamide therapy.

Appendix A includes yearly tables showing details of the numbers of empyemata at the various ages, with the bacteriological types. The yearly figures are then combined into two tables, one showing the whole age group covered, 0 to 14 years, and another the selected age group of 0 to 2 years, which is the most critical group when considered in regard to mortality rate.

Discussion of Tables

From a study of the tables in Appendix A it will be seen that although the admissions of acute pneumonia for the two five-year periods show a fall (from 2,067 to 1,686), by comparison the reduction of the empyema incidence is much more pronounced (from 192 to 63). A large part of this reduction is due to the effect of sulphonamide therapy upon the clinical course of acute pneumonia. The effect on the pneumococcal and streptococcal types is most striking, but the effect upon the staphylococcal cases is noticeable only in the group over two years of age. There appears to be little or no change either upon the incidence or mortality in the group 2 years of age and under.

The increased mortality rate in the sulphonamide cases is difficult to explain accurately. Some cases were extremely ill on admission, and it is probable that, of these, a number were inadequately treated with sulphonamides. The post-mortem examinations not infrequently revealed lesions other than empyemata. Pericarditis occurred in two cases, the empyema was bilateral in one case, meningitis occurred in one case, and congenital pyloric stenosis was present in another. Post-mortem examinations were not carried out on all fatal cases.

The effect upon the staphylococcal cases is shown to be fairly adequate control of the pneumonic process in the group 2 to 14 years. This effect is lacking in the under 2 years group, and this fact is of great importance, since now the incidence of staphylococcal empyema is at least as great, if not greater, than the pneumococcal types. In the cases 2 years and under a general mortality rate of some 64 per cent. exists, indicating that empyema in a child of 2 years of age is a serious condition, whatever the causal organisms.

Summary of Conclusions

A study of the tables in Appendix A shows the following results obtained over the period 1934-45:

1. Reduction in pneumococcal and streptococcal empyemata in children and infants.

2. Reduction of staphylococcal empyemata in children of 2 to 14 years; little or no effect either on the number of cases or mortality in the group 0 to 2 years.

3. Staphylococcal cases are at least as frequent, if not slightly more frequent, than pneumococcal cases in the group 0 to 2 years.

4. A general mortality rate in the 0 to 2 years group for all bacterial types is 64 per cent.

Staphylococcal Pneumonia and Empyema

Because of the increasing importance of pneumonia and empyema due to the Staphylococcus aureus, a review of these conditions is now included.

The Staphylococcus aureus has long been known as a secondary invading organism in influenza epidemics. Chickering and Park (1919) reported a series of 155 cases of this type. The mortality rate was appalling, and only two of the patients recovered. Of the 153 fatal cases, a frequent post-mortem finding was the occurrence of multiple abscesses in the pneumonic areas. Cultures revealed the Staphylococcus aureus.

The recognition of a primary staphylococcal pneumonia was largely due to the efforts of Reimann, H. A. (1933), who described six cases of primary staphylococcal pneumonia in children. Of two fatalities in this short series, one occurred in an infant. He stated that the clinical picture was suggested in pneumonia cases by the following features: (1) the severity of the illness, (2) the occurrence of rigors, (3) sweating, (4) a remittent septic temperature, and (5) a very high polymorphonuclear-leucocytosis. To these clinical observations is now added sulphonamide resistance, which also helps in the diagnosis. The examination of the sputum or lung puncture specimen may help in the diagnosis, but often the results are not conclusive. The difficulty of obtaining sputum from infants or children frequently renders the specimen of little value; and lung puncture is not without risk, particularly in staphylococcal cases. In adults, sputum examination is reliable and shows Staphylococcus aureus as the predominating organism. Reimann suggests that the Staphylococcus aureus, a normal inhabitant of the respiratory tract, becomes active when resistance is lowered by influenza, malnutrition, or some chronic disease, e.g. nephritis.

In most reported series of empyemata in children, it was the custom to record the number of cases due to the different bacteria responsible. Although cases of empyemata produced by the Staphylococcus aureus were often included, the significance of the relatively large numbers of such cases was not stressed until 1935.

Neuhof and Berck (1935) noted the high incidence of empyemata due to the Staphylococcus aureus in infants. The lesion, which often lead to pleural spread, was recognized as the sub-pleural abscess. This lesion was seen in many fatal cases. Smith, C. M. (1935), has described four cases of fulminating pneumonia in infants in a maternity block. All were due to the Staphylococcus aureus and were the probable result of a carrier state of Staphylococcus aureus amongst the staff and children.

MacGregor, A. R. (1936), in a detailed account of ten post-mortem examinations, supports the claim of Reimann that a true primary staphylococcal pneumonia does exist. Full reports of ten fatal cases of staphylococcal pneumonia are given. The cases occurred between August, 1935, and May, 1936. All cases were in children, the ages being from sixteen days to three and a half years, and eight were children of under one year. In four cases sero-fibrinous pleurisy had occurred, culture revealing the presence of Staphylococcus aureus. Six cases had definite empyemata, and of these three showed pyopneumothorax. All cases showed the lung as the primary focus of staphylococcal infection. Mixed organisms were found only when bronchopleural fistula had occurred. In these cases the Staphylococcus aureus was the predominating organism. Lesions were frequently related to one lobe of a lung. They were usually small, often surrounded by a haemorrhagic zone, and the centre of the area was red or yellow according to the duration of the lesion. In some cases liquefaction to pus had occurred. Sections of the affected area showed the bronchial route as the mode of entry, and the bronchus was often occluded in the pneumonic process. Adjacent bronchi showed inflammatory reaction, but this was not generalized in the remainder of the lungs. When the process passed to suppuration the result depended largely on the position of the pneumonic area. Rupture into the pleura was common, and in three cases a patent bronchus was also eroded, when a bronchopleural fistula resulted. One of the cases was related to the inhalation of milk.

Since MacGregor's excellent report appeared there have been frequent references to the condition in the journals of children's diseases, and much attention has been given to this subject, in American journals in particular. Hochberg and Kramer (1939) reviewed 300 cases of empyemata in children and infants. In this series of cases thirty-three due to the Staphylococcus aureus were included. Thirteen deaths occurred in all (40 per cent. mortality), and cases two years and under numbered seventeen, with eight deaths, 47 per cent. mortality.

Amongst the 300 cases discussed, 255 are presented with full details of the causal organisms. These cases may be compared with those now presented which occur in the 1934-38 period (table 1), and a similarity of the relative frequency of staphylococcal cases is shown, although a lower mortality rate is present in the series of Hochberg and Kramer.

TABLE 1

COMPARISON BETWEEN HOCHBERG AND KRAMER'S AND CHAPLIN'S CASES

	0–15 years	Deaths	0–2 years	Deaths	% Incidence 0–15	% Incidence 0–2
Hochberg and Kramer	33	13	17	8	13	24
Mortality	40%		47%			
	0–14 years	Deaths	0–2 years	Deaths	% Incidence 0–14	% Incidence 0–2
A. E. Chaplin ..	23	11	14	9	12	20
Mortality	48%		64%			

In the same year Kanof, et al. (1939), reported a mixed series of primary and secondary staphylococcal empyemata. Twenty-five cases of primary empyemata were included in a total of thirty-seven. Sixteen of the primary cases occurred in the group one year and younger, with eleven deaths (70 per cent. mortality). Hochberg and Steiner (1940) showed the high incidence of staphylococcal cases in a report of the post-mortem findings on nineteen fatal cases of empyemata. All the patients were infants of three months age or less, and bacteriological data was included for twelve of this group: eight of the twelve were due to the Staphylococcus aureus.

In a research into post-mortem specimens, Gaspar (1941) found that in pneumonia in children at least 25 per cent. of cases were caused by the Staphylococcus aureus. Clemens, H. H., and Weens, H. S. (1942), pointed out that pyopneumothorax was a frequent complication in this particular type of empyema, and noted its occurrence in four out of six fatal cases reported.

Details of a single case of Staphylococcal pneumonia showing resistance to sulphonamide therapy was described by Genninger (1943). The development of empyema, a description of the fatal outcome of the case, and full details of post-mortem findings are given. The empyema was the sequel to the rupture of a sub-pleural abscess in the pneumonic area.

In a further series of surgically treated cases (primary and secondary in type), Ladd and Swan (1943) reported seventeen primary cases, all of one year and under, in which seven deaths occurred. (The seven fatal cases were aged four months or younger.)

A review of twenty-nine cases of staphylococcal empyema admitted to a babies' hospital from 1922 to 1942 was made by Riley (1944). Nine, with five deaths (55 per cent. mortality), occurred in the pre-sulphonamide era; between 1938 and 1942 there were twenty, with five deaths (25 per cent. mortality). In this series a relative increase in the occurrence of staphylococcal cases was noted in the sulphonamide era, this fact agreeing with the figures presented previously.

TABLE 2

SUMMARY OF FIVE SERIES OF CASES OF EMPYEMA

Authors	Cases	Deaths
Hochberg and Kramer, 1939 ..	33	13
Kanof, Kramer, and Carnes, 1939	16	11
Clemens and Weens, 1942	6	6
Ladd and Swan, 1943	33	18
Riley, 1944	29	10
Totals	117	58 (49·5%)

All the authors stress the seriousness of the condition, particularly when it occurs in children of two years and younger. In the first six months of life the prognosis is extremely poor. American observers have sought to link these facts with experimental findings. Kobak and Pilot (1931) have shown that newborn children fail to give positive reactions to intradermal injections of staphylococcal filtrate. A gradual increase in positive reactions was noted, until at one year 75 per cent. of children reacted.

It has also been noted that, although a high antihaemolysin is present at birth, there is a rapid fall, with none detectable at the age of two months. A gradual rise in titre occurs from this period onwards (Bryce and Burnett, 1932). It is probable that these findings have some importance in determining the seriousness of the disease at the age group mentioned.

TABLE 3

SUMMARY OF CASES UNDER TWO YEARS IN FOUR SERIES OF CASES OF EMPYEMA

Authors	Cases	Deaths	Age
Hochberg and Kramer, 1939.	17	8	0–2 years
Kanof, Kramer and Carnes, 1939.	16	11	0–1 year
Ladd and Swan, 1943	17	7	0–1 ,,
Riley, 1944	22	8	0–1 ,,
Total	72	34 (47·2%)	

TABLE 4

STAPHYLOCOCCAL CASES IN THE PRESENT SERIES

Year	0–14 years	Deaths	0–2 years	Deaths
1934	5	2	3	2
1935	3	2	3	2
1936	4	2	2	1
1937	5	2	3	2
1938	6	3	3	2
Total	23	11	14	9
1939	2	1	2	1
1940	2	2	2	2
1941	5	3	4	3
1942	4	3	4	3
1943	4	2	4	2
1944	3	1	3	1
Total	18	11	17	11
Jan. 1945	2	2	2	2
Total Cases	45	25 (55·5%)	35	23 (64·5%)

Table 2 gives a summary of the above-mentioned series. The mortality (49·5 per cent.) is somewhat lower than the mortality rate in the series now presented, i.e., forty-five cases, twenty-five deaths, mortality 55·5 per cent.

In the present survey forty-five cases of staphylococcal empyemata are reviewed, these comprising all admissions of this type from 1934 to January, 1945, and they are included in the author's general list previously reviewed. These forty-five cases are the two groups of presulphonamide and sulphonamide cases. Thirty-five are cases under two years of age, and in this group twenty-three deaths occurred, a mortality of 64·5 per cent. This figure shows an increase when compared with the cases under two years of age in the previously mentioned series (table 3). Table 4 shows the details of the pre-penicillin staphylococcal cases in the present series.

PART II

USE OF PENICILLIN IN THE TREATMENT OF SULPHONAMIDE-RESISTANT PNEUMONIA, AND IN EMPYEMA THORACIS DUE TO PENICILLIN-SENSITIVE ORGANISMS

With the discovery of penicillin by Fleming (1929), and its subsequent extraction by Chain, Florey, et al. (1940), at Oxford, an antibiotic became available for use in treatment of infections due to penicillin-sensitive organisms. Following the early clinical trials of Abrahams et al. (1941), and Florey and Florey (1943), the value of this new therapeutic agent was clearly established. Since empyemata following acute pneumonia are frequently produced by sensitive organisms, it is not surprising that penicillin has been used in the treatment of such cases. The staphylococcus, streptococcus, and pneumococcus are usually sensitive to penicillin, and hopes were held of its successful application in the treatment of empyemata due to these organisms. With the high mortality in the cases occurring in the first two years of life, and since the organism most commonly met at this period was the Staphylococcus aureus, it was felt that penicillin would play an important part in the treatment of such cases, particularly when this organism usually is sulphonamide-resistant.

In the days when penicillin was in short supply, cases that could be treated by local application were preferred to cases requiring systemic administration. Christie and Garrod (1944) mentioned sixteen cases of empyema in which one or two injections of 15-30,000 units of penicillin was all that was required to sterilize the pus in the pleural cavity. A marked reduction in the general toxicity was noticed. Butler, Perry and Valentine (1944) in a paper on the treatment of acute empyema with penicillin, confirmed the belief of Christie and Garrod that sterilization of the pleural pus made a consequent reduction in general toxaemia of the patient. They found, in treating seventeen cases of acute empyema, that it was not possible to cure these patients by aspiration and penicillin instillation alone. Rib resection was required to evacuate a sterile abscess. The removal of fibrin was necessary to prevent thickened pleura and deformity of the chest wall. These facts were confirmed by Keefer et al. (1943), Bennett and Parkes (1944), Dawson and Holly (1944), Herrell (1944), and Bloomfield et al. (1944).

The prophylactic instillation of penicillin in chest injuries with haemothorax was found by D'Abreu et al. (1944) to be of great value; frequently the sepsis was controlled with aspiration alone, and operation was avoided in some instances. Dawson and Holly (1944) included one case, an adult woman with an acute empyema due to the Staphylococcus aureus. She received intrapleural and systemic penicillin, and no surgical interference was necessary. Keefer et al. (1943) found it necessary to have a rib resection performed in seven out of nine cases treated with penicillin. They also found that penicillin could not be detected in the pleural cavity after large systemic doses had been administered.

Bennett and Parkes (1944) noted the excellent response of post-influenzal staphylococcal pneumonia to penicillin. The cure of an infant of ten months with a staphylococcal empyema by intrapleural and systemic penicillin was also included. This case had some residual thickened pleura, however. Some cases of staphylococcal pneumonia do respond to sulphonamides, as was shown by Michael (1942), who reported three recoveries in five cases of post-influenzal staphylococcal pneumonia when sulphadiazine was used. McBride (1944) reports the successful use of penicillin in two cases of staphylococcal pneumonia in infants. One child was four weeks old, the other five weeks, and both were desperately ill with pneumonia. No response was made to sulphonamides, but dramatic recoveries occurred when systemic penicillin was given.

The treatment of acute empyemata in children and infants presents an urgent problem. With such a high mortality due to all types of organisms it is not surprising that penicillin has been used extensively in treatment.

Gairdner (1944) reports a single case of pyopneumothorax due to Staphylococcus aureus in an infant. Pyaemia had followed intravenous infusion

of saline. This infant, although only four weeks old, recovered with intercostal drainage and heavy doses of sulphathiazole, and its recovery **without** penicillin is remarkable. Philips and Kramer (1945) reported five cases of empyema due to Staphylococcus aureus in infants of under one year of age. All cases received intrapleural and systemic penicillin, and only one death occurred. The fatal case was a child almost moribund on admission. Of the four cases which recovered, two were treated by aspiration alone, but the other two required surgical drainage to secure a good result, even though the pus had been sterilized.

Harris and Platou (1945) recorded a successfully treated case of pyopneumothorax in a premature baby twenty days old (a four-weeks premature Caesarian baby). When taken ill with pneumonia the response to both sulphadiazine and sulphamezathine was disappointing, and the child was gravely ill. After seven days' illness a pyopneumothorax was discovered, and the causal organism was the Staphylococcus aureus. Intrapleural penicillin (four occasions, 3,000 units) and systemic penicillin were sufficient to produce a complete recovery without surgical interference.

The difficulty experienced when aspiration is attempted as the sole method of interference is due to fibrin present in the pus blocking the lumen of the needle. The excessive fibrin production may be explained as a result of the experimental work of Dixon (1945). He discovered that although the staphylococcus normally produces two ferments, a coagulase and a fibrinolysin, in the presence of penicillin the second ferment is not liberated, although coagulase is still produced. Thus it is probable that a much slower absorption of fibrin occurs due to the absence of fibrinolysin.

Twenty-one Cases of Acute Empyema in Infants and Children Treated with Penicillin

The author has collected from three Birmingham hospitals a series of twenty-one children and infants with empyema; all received intrapleural penicillin therapy, and some were surgically drained as well. The causal organism in each case was duly tested for penicillin sensitivity, and all were found to be sensitive. One fatal case occurred, and at post-mortem examination the lung was expanded and normally aerated, and the surface of the lung was covered only by a thin layer of fibrin. Table 5 tabulates the cases according to age and bacteria responsible, and Appendix B gives details of cases.

This short series of cases further confirms the belief previously expressed, of the frequency of staphylococcal empyemata in the first two years of life. It is particularly significant that all cases under six months of age were due to this organism.

TABLE 5

THE PRESENT SERIES TABULATED ACCORDING TO AGE AND BACTERIA RESPONSIBLE

Age	No. of cases	Staph'l.	Pneumo'l.	Strept.
0–6 months ..	5	5	0	0
6–12 months	4	2	2	0
1–2 years ..	7	3	3	1
Over 2 years ..	5	2	3	0
Totals ..	21	12	8	1

MORTALITY RATE. From consideration of the five-year period of sulphonamide therapy, a general mortality figure of 60 per cent. was to be expected for the first two years of life, but in all the penicillin cases now presented only one fatality occurred (case 5). This patient was a child of four months of age who had its empyema treated by aspiration and penicillin instillation. The organism responsible was the Staphylococcus aureus. The case was complicated from the commencement by the presence of bilateral otitis media, and although the empyema was satisfactorily treated, the child developed bilateral mastoiditis and died from a severe gastro-enteritis. This terminal condition was not relieved either by operative interference to the mastoiditis, or by saline infusion. Post-mortem examination confirmed the clinical belief that the empyema had been treated adequately. The affected lung was re-aerated and was covered only by a thin fibrinous exudate. It could be claimed, therefore, that the empyema had been satisfactorily treated by penicillin, which had been given by the systemic route and by intrapleural injection.

CASES TREATED BY ASPIRATION ENTIRELY. In view of the reported difficulty experienced in securing complete resolution of an empyema by aspiration alone, it is significant that this method was successful in eight cases. One of these patients probably had a small interlobar collection of pus (case 17) and this case, while still in hospital, appears to be recovering satisfactorily. Case 21 had pus aspirated from the chest on one occasion only, and the empyema must have been small and localized. The other six cases (5, 6, 7, 8, 9, and 16), all had repeated aspiration of the pus in the pleural cavity and received both systemic and intrapleural penicillin. It is possibly significant that all except one of these latter six cases were under one year of age. This one case (case 8), although successfully treated by this method, had some thickening of the pleurae with a flattening of the corresponding side of the chest.

CASES NEEDING SURGICAL INTERFERENCE. In case 10, because of difficulty in deciding whether the

empyema had been completely dealt with, a rib resection was carried out; and, although no pus was discovered, a fair amount of free fibrin in a serous fluid was present, and also considerable thickening of the pleura. When the fibrin was removed, a short period of drainage was all that was necessary before the wound healed completely.

An example is presented by case 11, which illustrates the probable result of persistence with aspiration and penicillin instillation, although the size of the empyema remains stationary and the physical signs in the chest do not improve. Three weeks of such treatment had produced, in this particular case, marked flattening of the affected side of the chest and a scoliosis to the opposite side. The cause of this failure was revealed at operation. The chronic empyema, although sterile, contained one pint of pus and half a pint of fibrin, and both visceral and parietal pleurae were covered with a thick layer of fibrin. The empyema was treated by decortication and the cavity drained. The wound rapidly healed, but the deformity is still present, and the ultimate outlook remains uncertain. It is not unreasonable to assume that similar cases would need thoracoplasty to obliterate a cavity which the lung, because of the thickened pleura, is unable to expand and fill.

All the remaining patients were treated either by rib resection or intercostal drainage, after preliminary penicillin therapy had greatly improved their general condition. This treatment often resulted in the early sterilization of the pleural pus. Surgical drainage was usually followed by a speedy convalescence and rapid healing of the chest wound. Re-expansion of the lung was early and complete. Systemic penicillin given post-operatively appeared to help in producing an early cessation of discharge from the pleural cavity. This favourable result agrees with the experience of Roberts et al. (1945), who reported the necessity of surgical interference in the treatment of acute empyema in adults. Penicillin had failed to cure the empyema completely, and a sterile collection of pus had to be evacuated from the chest in most cases.

In twelve out of thirteen patients in the present series who received surgical treatment as well as penicillin therapy, details are available of the time taken for complete healing of the chest wound. (One case remains in hospital with a drainage tube still present.) The average time for complete healing was 5·5 weeks, which is an extremely satisfactory result.

Failure of aspiration alone to cure thirteen out of the twenty-one patients agrees with the experience of Butler et al. (1944), Keefer et al. (1943) and Roberts et al. (1945). The extremely low mortality rate in this series of cases confirms the hope expressed by Philips and Kramer (1945) of a marked improvement due to the application of penicillin therapy. Dosages of penicillin for the interpleural route, instead of from 10,000 to 30,000 units, should be somewhat higher, according to the recommendations of Keefer et al. (1945).

RADIOGRAPHS. Eight radiographs, from three of the patients in this series, are reproduced. A case is illustrated from each of the two groups, i.e., aspiration alone, and aspiration followed by surgical drainage. Films at the commencement of treatment and at the end of treatment are shown to illustrate the good result in each type of case. In the surgically treated case an additional intermediate film is included, showing the drainage tube in situ. Three radiographs are included from case 11. The first illustrates the condition of the chest at the commencement of penicillin therapy, the second shows the failure of penicillin with aspiration to produce resolution of the empyema. Scoliosis and flattening of the chest have developed. The third film shows the improvement brought about by decortication of the empyema following resection of portions of two ribs. (See Plates VI and VII.)

BACTERIOLOGY. When the patients are reviewed with regard to the bacterium responsible, apart from the bacteriological examination of the pus, only slender clinical features help in differentiation of the cases. The onset of the empyema is not conclusive in suggesting a particular bacterium to be responsible, but the occurrence of an empyema within the first week of illness suggests the Staphylococcus aureus as the probable cause. This is illustrated by cases 7, 8, 9 and 14. When cases occurring in the first six months of life are studied, the staphylococcal cases predominate. In the series now under review, five cases under six months of age are included, and all were caused by this organism.

The presence of cyanosis and working alae nasi is common to all types of empyema.

It was noticed that the pus in staphylococcal cases was frequently blood-stained at the commencement, and this feature could be explained by the rupture of a sub-pleural abscess into the pleural cavity accompanied by a small amount of haemorrhage.

Resistance of the pneumonic state to sulphonamides does not necessarily mean that the staphylococcus is the causal organism, although that is often the case. In the series now presented, two cases showing marked resistance to sulphonamide subsequently developed pneumococcal empyemata (cases 18 and 19).

A feature common to all bacterial types in the twenty-one cases was the excellent response to penicillin therapy. Although a 60 per cent. mortality rate existed in the pre-penicillin era in cases two years of age and under, in the present series no fewer than sixteen fall within this age group, with only one fatality. In this fatal case the lung lesion and empyema had been cured, the cause of death being a fulminating gastro-enteritis following acute mastoiditis.

Conclusions

Penicillin plays an important part in the treatment of acute empyemata due to sensitive organisms. The penicillin is given by parenteral and intrapleural routes. Aspiration of the pleural pus, with instillation of an adequate dose of penicillin every two to three days, may produce complete resolution of the empyema in cases up to one year of age.

From one year onwards, success by this method is unlikely, unless the empyema is small. The aspirations are controlled by frequent radiographic examination; and, should the response of the case be slow, with possible development of a thickened pleura, surgical drainage is indicated. Similar interference is indicated when fibrin in the pus prevents adequate removal by aspiration. The intrapleural injection of penicillin should produce sterility of the pleural pus after one or two aspirations.

The rapid recovery with shortened convalescence is noted in both groups of cases, i.e., with or without surgical drainage.

Features which support the probable diagnosis of staphylococcal empyema include: (1) the onset of empyema within the first week of illness; (2) a patient less than six months of age; (3) resistance of the pneumonia to sulphonamides; (4) a blood-stained specimen of pus obtained on aspiration of the pleural cavity.

Summary

1. In the introduction a general review of the literature on empyema thoracis is given. The problem of such cases in children and infants is stressed.

2. An analysis of 275 cases of empyemata in children and infants is made with regard to age, mortality, and bacteriological date. Two five-year periods, one of ' non-sulphonamide,' and the other of ' sulphonamide ' therapy, are compared. The value of sulphonamides in the prevention of post-pneumonic empyemata is assessed. The resistance of staphylococcal cases to sulphonamide is shown.

3. Literature on staphylococcal pneumonia and empyema is reviewed with regard to incidence and mortality rates.

4. The use of penicillin in the treatment of sulphonamide-resistant pneumonia and in empyema due to sensitive organisms is reviewed.

5. A collected series of twenty-one cases of penicillin-treated empyemata in children and infants is presented. Good results are reported, with one fatal case in the whole series. The limitations of treatment of acute empyema in children and infants by aspiration and penicillin alone are discussed. The need for surgical drainage in many cases is shown.

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(References continued on p. 101)

APPENDIX A

Details of Cases of Empyema at Various Ages

AGE (Years)	1934						1935						1936						1937						1938					
	Pneum.	Deaths	Strep.	Deaths	Staph.	Deaths	Pneum.	Deaths	Strep.	Deaths	Staph.	Deaths	Pneum.	Deaths	Strep.	Deaths	Staph.	Deaths	Pneum.	Deaths	Strep.	Deaths	Staph.	Deaths	Pneum.	Deaths	Strep.	Deaths	Staph.	Deaths
0– 1	3	3	–	–	3	2	4	2	2	2	2	2	5	4	2	2	2	1	5	3	2	2	1	1	2	1	3	3	3	2
1– 2	2	0	–	–	–	–	4	1	2	1	1	0	2	0	–	–	–	–	4	1	3	2	2	1	9	3	1	0	–	–
2– 3	3	0	–	–	–	–	3	1	1	0	–	–	1	0	1	0	–	–	2	0	–	–	–	–	5	1	1	0	–	–
3– 4	5	0	1	1	1*	0	3	0	–	–	–	–	2	0	1	0	–	–	2	2	–	–	1	0	2	0	–	–	–	–
4– 5	4	0	–	–	–	–	2	0	1	0	–	–	3	0	1	0	–	–	2	0	–	–	1	0	4	0	1	0	–	–
5– 6	6	0	–	–	–	–	2	0	1	0	–	–	3	0	–	–	–	–	2	0	–	–	–	–	5	1	1	0	1	0
6– 7	3	1	–	–	–	–	3	0	–	–	–	–	–	–	1	0	1	0	1	0	–	–	–	–	4	0	–	–	–	–
7– 8	2	0	–	–	–	–	2	0	–	–	–	–	–	–	1	0	–	–	1	0	–	–	–	–	1	0	1	0	1	1
8– 9	1	0	1	0	–	–	1	0	–	–	–	–	1	0	–	–	1	1	–	–	1	0	–	–	–	–	–	–	–	–
9–10	1	0	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1	0	–	–	–	–
10–11	–	–	1	0	–	–	1	0	–	–	–	–	–	–	–	–	–	–	1	0	–	–	–	–	1	0	–	–	–	–
11–12	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1	0	–	–	–	–	–	–	–	–	1	0
12–13	1	1	1	0	–	–	2	1	1	0	–	–	1	0	–	–	–	–	1	0	–	–	–	–	–	–	–	–	–	–
13–14	–	–	–	–	1*	0	1	0	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Total	31	5	4	1	5	2	28	5	8	3	3	2	18	4	7	2	4	2	22	6	6	4	5	2	34	6	8	3	6	3

Besides the above figures, the following cases of mixed organism, with no deaths, were reported: 1935, age 1-2 years, 1 case; age 11-12 years, 1 case; 1936, age 2-3 years, 1 case.

Age	1934			1935			1936			1937			1938		
	Total Cases	Deaths	%	Total Cases	Deaths	%	Total Cases	Deaths	%	Total Cases	Deaths	%	Total Cases	Deaths	%
0–14	40	8	20·0	41	10	24·4	30	8	26·6	33	12	36·4	48	12	25·0
0– 2 All	8	5	62·5	16	8	50·0	11	7	63·6	17	10	58·8	18	9	50·0
0– 2 Staph.	3	2	66·6	3	2	66·6	2	1	50·0	3	2	66·6	3	2	66·6
A.P.	462			359			321			429			496		
E.	8·65%			11·4%			9·3%			7·7%			9·6%		

APPENDIX A (continued)

AGE (years)	1939						1940						1941						1942						1943						1944					
	Pneum.	Deaths	Strep.	Deaths	Staph.	Deaths	Pneum.	Deaths	Strep.	Deaths	Staph.	Deaths	Pneum.	Deaths	Strep.	Deaths	Staph.	Deaths	Pneum.	Deaths	Strep.	Deaths	Staph.	Deaths	Pneum.	Deaths	Strep.	Deaths	Staph.	Deaths	Pneum.	Deaths	Strep.	Deaths	Staph.	Deaths
0– 1	1	0	–	–	1	1	2	2	–	–	1	1	2	1	1	1	3	2	1	1	–	–	4	3	1	1	–	–	3	1	1	1	1	1	3	1
1– 2	1	0	1	0	1	0	1	0	–	–	1	1	1	0	–	–	1	1	4	2	–	–	–	–	2	1	–	–	1	1	–	–	–	–	–	–
2– 3	3	0	–	–	–	–	1	0	–	–	–	–	–	–	–	–	1	0	3	3	–	–	–	–	1	0	–	–	–	–	–	–	2	1	–	–
3– 4	4	0	1	0	–	–	–	–	–	–	–	–	3	0	–	–	–	–	2	0	–	–	–	–	1	0	–	–	–	–	–	–	–	–	–	–
4– 5	3	1	–	–	–	–	–	–	–	–	–	–	1	0	–	–	–	–	–	–	–	–	–	–	1	0	–	–	–	–	–	–	–	–	–	–
5– 6	2	0	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1	0	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
6– 7	1	1	–	–	–	–	1	0	–	–	–	–	–	–	–	–	–	–	1	0	–	–	–	–	1	0	–	–	–	–	–	–	–	–	–	–
7– 8	–	–	–	–	–	–	–	–	1	0	–	–	–	–	–	–	–	–	1	0	–	–	–	–	–	–	–	–	–	–	1	0	–	–	–	–
8–10	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1	0	–	–	–	–
10–12	–	–	–	–	–	–	–	–	–	–	–	–	1	1	–	–	–	–	–	–	1	0	–	–	–	–	–	–	–	–	–	–	–	–	–	–
12–14	1	0	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Total	16	2	2	0	2	1	5	2	1	0	2	2	8	2	1	1	5	3	13	6	1	0	4	3	7	2	0	0	4	2	3	1	3	2	3	1

One fatal case of mixed organism occurred in 1943 in the age group 13-14. One non-fatal case of mixed organism occurred in 1944 in the age group 2-3 years.

AGE	1939			1940			1941			1942			1943			1944		
	Total Cases	Deaths	%	Total Cases	Deaths	%	Total Cases	Deaths	%	Total Cases	Deaths	%	Total Cases	Deaths	%	Total Cases	Deaths	%
0–14	20	3	15·0	8	4	50·0	14	6	42·8	18	9	50·0	12	5	41·7	11	4	36·3
0– 2 All	5	1	20·0	5	4	80·0	8	5	62·5	9	6	66·6	7	4	57·1	5	3	60·0
0– 2 Staph.	2	1	50·0	2	2	100·0	4	3	75·0	4	3	75·0	4	2	50·0	3	1	33·3
A.P.	347			320			400			328			372			266		
E.	5·6%			2·5%			3·5%			5·5%			3·23%			4·1%		

A.P. = Cases of acute pneumonia.
E. = Incidence of empyema.
* = few streptococci.

APPENDIX A (continued)

SUMMARY OF ALL CASES, 1934–45

Year	Pneumococcal		Streptococcal		Staphylococcal		Mixed organisms		Totals	
	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths
1934	31	5	4	1	5	2	–	–	40	8
1935	28	5	8	3	3	2	2	0	41	10
1936	18	4	7	2	4	2	1	0	30	8
1937	22	6	6	4	5	2	–	–	33	12
1938	34	6	8	3	6	3	–	–	48	12
Total	133	26	33	13	23	11	3	0	192	50
Mortality	19·5%		39·4%		48·0%		–		26·0%	
1939	16	2	2	0	2	1	–	–	20	3
1940	5	2	1	0	2	2	–	–	8	4
1941	8	2	1	1	5	3	–	–	14	6
1942	13	6	1	0	4	3	–	–	18	9
1943	7	2	–	–	4	2	1	1	12	5
1944	3	1	3	2	3	1	2	0	11	4
Total	36	13	6	3	18	11	3	1	63	28
Mortality	36·1%		50·0%		61·1%		33·3%		44·4%	

Total cases = 275.

% Incidence

Period	Pneumococcal	Streptococcal	Staphylococcal	Mixed organisms
1934–8	69·2	17·2	12·0	1·6
1940–4	57·1	9·5	28·6	4·8

SUMMARY OF CASES UNDER TWO YEARS, 1934–45

Year	Pneumococcal		Streptococcal		Staphylococcal		Mixed organisms		Totals	
	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths
1934	5	3	0	0	3	2	–	–	8	5
1935	8	3	4	3	3	2	1	0	16	8
1936	7	4	2	2	2	1	–	–	11	7
1937	9	4	5	4	3	2	–	–	17	10
1938	11	4	4	3	3	2	–	–	18	9
Total	40	18	15	12	14	9	1	0	70	39
Mortality	45·0%		80·0%		64·3%		–		55·7%	
1939	2	0	1	0	2	1	–	–	5	1
1940	3	2	–	–	2	2	–	–	5	4
1941	3	1	1	1	4	3	–	–	8	5
1942	5	3	–	–	4	3	–	–	9	6
1943	3	2	–	–	4	2	–	–	7	5
1944	1	1	1	1	3	1	–	–	5	3
Total	15	9	2	2	17	11	–	–	34	23
Mortality	60·0%		100·0%		64·7%		–		67·6%	

Total cases = 109

% Incidence

Period	Pneumococcal	Streptococcal	Staphylococcal	Mixed organisms
1934–8	57·1	21·4	20·0	1·5
1940–4	44·1	5·9	50·0	–

EMPYEMA INCIDENCE RATES

Year	Acute pneumonia	Empyemata	% Incidence
1934	462	40	8·65
1935	359	41	11·4
1936	321	30	9·3
1937	429	33	7·7
1938	496	48	9·6
Total	2,067	192	9·3
1939	347	20	5·8
1940	320	8	2·4
1941	400	14	3·25
1942	328	18	5·5
1943	372	12	3·23
1944	266	11	4·1
Total	1,686	63	3·7

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APPENDIX B.

Case No.	Age in years	Sex	Relevant history	Condition on admission	Day of onset of empyema	Organism	Treatment
1	1½	F	Ill for 7 days with cough and dyspnoea; worse for 1 day.	Well nourished; febrile, grunting respiration; impairment note, Rt. base, ? pneumonia.	14	Staphylococcus C + P.S.	Sulphonamides (resistant); aspiration and intrapleural penicillin; systemic penicillin and surgical drainage.
2	1	F	Ill for 2 days with cough and dyspnoea.	Well nourished; ill; grunting respiration; febrile; impaired note Rt. base; ? pneumonia.	8	Staphylococcus C + P.S.	Sulphonamides, good response; the empyema developed and was treated by aspiration and instillation of penicillin and, later, surgical drainage.
3	1 3/12	F	Cough and febrile for 3 days.	Well nourished; febrile; marked dyspnoea; impaired note; ? bronchial breath sounds; Rt. upper lobe.	16	Staphylococcus C + P.S.	Initial response to sulphonamides; relapse and empyema developed; aspiration and instillation of penicillin, then rib resection.
4	1 4/12	M	Cough, dyspnoea 1 day.	Well nourished; ? pneumonia right base.	10	Staphylococcus C + P.S.	Sulphonamide and penicillin—resistant pneumonia; empyema developed; initial aspiration and instillation of penicillin; rib resection (large empyema).
5	4/12	F	Cold for 1 week; febrile; wheezy chest; off feeds; otitis media (bilateral) 12 days before onset of present illness.	Fairly well nourished; febrile; acute upper respiratory infection and bilateral otitis media.	23	Staphylococcus C + P.S.	Initial sulphonamide therapy, no response; developed extensive sulphonamide-resistant pneumonia (right base); empyema treated by aspiration and by instillation and systemic penicillin.
6	10/12	F	Ill for 9 days with cough, feverish over similar period.	Fairly well nourished; febrile; signs of fluid at Rt. base; aspiration—pus +.	10	Staphylococcus C + aureus P.S.	Aspiration of pus with instillation of 20,000 × 5 systemic penicillin.
7	1/12	M	Cough 3-4 days; attacks of cyanosis.	Poorly nourished; extremely ill; dull at Rt. base, ? fluid; aspiration—pus +.	5	Staphylococcus C + aureus P.S.	Repeated aspiration of pus with intrapleural penicillin 20,000 × 5; systemic penicillin; sulphadiazine.
8	2 11/12	M	Tiredness for 4 days with pain in back; cough and dyspnoea for 1 day.	Fairly well nourished; febrile; grunting respiration; poor movement, left chest; dull left base, ? fluid; aspiration—pus +.	5	Staphylococcus C + aureus P.S.	Repeated aspiration of pus (9 times) and instillation intrapleural penicillin; systemic penicillin and sulphadiazine by mouth.
9	6/52	F	Cold for 3 days; vomiting all feeds.	Pale, wasted; cough; febrile; dullness and distant breath sounds, left base; ?pneumonia.	5	Staphylococcus C + aureus P.S.	Repeated aspiration of pus; penicillin instilled × 4; sulphadiazine by mouth.
10	2	M	Pneumonia; swinging temperature; pus aspirated from chest before admission (10th day).	Pale, toxic, febrile; dull and absent breath sounds, left chest; ? fluid; aspiration—pus +.	10	Pneumococcus P.S.	Repeated aspiration and instillation of penicillin; initial response to systemic penicillin, but relapsed with more fluid; resection and drainage for relapse; sulphadiazine and systemic penicillin given.
11	9	F	Ill for 9 days; tired and had shivering attacks; pain in left chest 3 days; cough for 2 days.	Pale, toxic, febrile; dull left base; ? fluid present.	9	Pneumococcus P.S.	Repeated aspiration of chest and intrapleural penicillin, 50,000 × 5; failure of resolution resulted in surgical interference.
12	7	M	Cough for 4 days; listless off food; no pain.	Fairly well nourished; febrile; dull right base distant breath sounds; ? pneumonia.	30	Pneumococcus P.S.	Sulphadiazine by mouth; no response of temperature or signs in chest; finally developed pus on 30th day of illness; aspiration and instillation of penicillin followed by rib resection.
13	1 1/12	F	Cough, swelling, and ulceration of gums for 1 week.	Fairly well nourished; ulcers in mouth; febrile; no signs of consolidation in chest.	4	B. Haemolytic Streptococci P.S.	After satisfactory treatment to mouth, and acute febrile illness had begun with signs in chest, right upper lobe, sulphadiazine was given; fluid developed 4th day; aspiration—pus; intrapleural penicillin × 2, followed by intercostal drainage.
14	3/12	M	Cough; feverish for 1 day; difficult breathing and off food 1 day.	Fairly well nourished; alae nasi +; febrile; no signs of consolidation.	4	Staphylococcus C + aureus P.S.	Signs of pneumonia, right base; sulphonamides given; no response; ? fluid right base, pus +; intrapleural penicillin × 5; sulphamezathine by mouth.

APPENDIX B.

Progress.	Radiograph	Features of case	Result
Relapse after rib resection, ? due to inadequate course of penicillin (systemic).	1: Pneumonia, right base. 2: Fluid right base. 3: Resolution proceeding. 4: Chest clear.	Sulphonamide-resistant pneumonia; satisfactory resolution of empyema; relapse due to too short post-operative course of penicillin.	Good: chest wound healed soundly.
Post-operative relapse due to inadequate course of penicillin (systemic).	1: Pneumonia, right base. 2: ? Fluid right base. 3: Resolving. 4: Chest almost clear. 5: Resolution complete.	Empyema developed after response to sulphonamides; post-operative relapse responded to systemic penicillin.	Good: chest wound healed soundly.
Good response to surgical drainage; although child improved with aspiration, no headway was made against size of empyema.	1: Shadow, apex right lung, ? pneumonia. 2: Opacity, right base, ? Fluid. 3: Resolution proceeding. 4: Chest clear.	Good response to penicillin; rapid resolution of empyema and early healing of chest wound.	Good: chest wound healed soundly.
Rapid response to penicillin instillation and finally rib resection. Early healing of chest.	1: Pneumonia, right middle lobe. 2: Extension to right lower lobe. 3: ? Fluid right base. 4: Resolution complete.	Empyema developed after sulphonamides and penicillin; rapid resolution of empyema after rib resection.	Good: rapid resolution and healing.
Empyema resolved satisfactorily; otitis showed no improvement; developed diarrhoea and vomiting and bilateral mastoiditis; no response to mastoidectomy.	Repeated x-rays showed gradual resolution of empyema before development of diarrhoea and vomiting.	Satisfactory treatment of empyema by aspiration alone; death from diarrhoea and vomiting and bilateral mastoiditis.	Although child died, necropsy revealed no pneumonia and complete resolution of empyema.
Gradual resolution of empyema with aspiration alone.	1: Fluid, right base. 2: Chest clearing. 3: Chest clear.	Satisfactory response of empyema without resection.	Good; no operation.
Rapid reduction of general toxicity of child; satisfactory resolution of empyema without surgical drainage.	1: Fluid, right base. 2: Chest clearing. 3: Chest clear.	Rapid initial reduction in general toxicity; satisfactory resolution with aspiration alone.	Good; no operation.
The empyema was large and resolved only with difficulty without operation; chest remained flattened, and some thickening of pleura was present.	1: Fluid, left chest. 2: Less fluid present. 3: Some residual thickening of pleura.	Empyema was large and responded with difficulty to aspiration alone; illness was somewhat prolonged, and some residual thickening of pleura remained.	Fair; some thickened pleura when discharged home.
Response to aspiration and instillation of penicillin; no systemic penicillin; sulphadiazine by mouth.	1: Fluid, left base. 2: Less fluid. 3: Chest almost clear.	Response to local penicillin and sulphadiazine; no operation or systemic penicillin.	Good: no operation.
Initial response to aspiration alone; relapsed with increase in size of empyema; rib resection performed; fibrin and serous fluid; not a true empyema; rapid healing following operation.	1: Fluid, left chest. 2: Less fluid. 3: Marked increase in fluid. 4: After operation chest clearing. 5: Chest almost clear.	Failure to respond to aspiration alone; rapid healing following surgical drainage.	Good after surgical drainage.
After initial response the empyema remained stationary; the chest became flattened, and scoliosis resulted.	1: Fluid, left chest. 2: Some reduction in extent of fluid. 3: More fluid. 4: Scoliosis and flattening of chest, with thickened pleura. 5: Rapid clearing after operation.	Failure of response to aspiration alone; early development of thickened pleura with flattening of chest and scoliosis; rapid healing following decortication of chronic empyema.	Fair: earlier operative interference may have prevented scoliosis and flattening of chest.
Sulphonamide-resistant pneumonia; late development of empyema; good response to penicillin; rapid recovery after rib resection.	1: Pneumonia, right base. 2: No change (repeated). 3: Fluid, right base. 4: Chest clearing.	Late development of empyema (large size) after sulphonamide-resistant pneumonia.	Good: healed after resection and drainage.
Developed pneumonia in hospital ? secondary to ulcerated mouth; rapid response after penicillin and intercostal drainage; relapse after 6 weeks, but resolved speedily on discharge of a superficial abscess in intercostal scar.	1: Satisfactory drainage of empyema. 2: Chest clearing. 3: Chest clear.	Response of empyema to aspiration and instillation of penicillin followed by intercostal drainage; no systemic penicillin given.	Good following intercostal drainage.
After repeated aspirations (5) the empyema did not appear to be resolving; intercostal drainage.	1: Pneumonia right base. 2: ? fluid, right base. 3: Chest clearing. 4: Chest clear.	Good result after aspiration and instillation of penicillin followed by intercostal drainage.	Good following intercostal drainage.

APPENDIX B—*continued.*

Case No.	Age in years	Sex	Relevant history	Condition on admission	Day of onset of empyema	Organism *	Treatment
15	1½	M	Ill for 3 weeks; cough and occasional vomiting.	Pale, poorly nourished; poor movement, left chest; dull ? fluid; aspiration—pus.	Present on admission to hospital.	Pneumococcus P.S.	Repeated aspiration of pus and instillation of penicillin (4); rib resection.
16	1 0/12	M	Ill 5 days; cough; vomiting; off feeds.	Pale; fat; alae nasi +; no consolidation; ? acute bronchitis.	9	Staphylococcus C + aureus P.S.	Pneumonia developed (right lower lobe); no response to sulphonamides; aspiration and instillation of penicillin.
17	1½	M	Ill for 3 weeks; cough and occasional vomiting; worse for 3 days; now off feeds.	Fairly well nourished; toxic; febrile; ? pneumonia, right upper lobe.	Doubtful	Pneumococcus P.S.	No true response to sulphonamides; penicillin given systemically and into ? interlobar empyema.
18	8/12	M	Ill 1 week; fretful; coryza and cough.	Poorly nourished; dyspnoea +; cyanosed and febrile; dull left base; bronchial breath sounds; ? pneumonia.	11	Pneumococcus P.S.	No response to sulphonamides; systemic penicillin; aspiration and intrapleural penicillin × 3, and then rib resection.
19	3½	F	Ill for 3 weeks with cold and cough; worse for 2 days.	Pale, spare; toxic; febrile; dull left lower lobe; bronchial breath sounds; ? pneumonia.	? 32	Pneumococcus P.S.	Good response to sulphonamide; relapse after 5 days—fluid found left chest; intrapleural penicillin × 2; large empyema—drainage by rib resection.
20	8/12	M	Ill 4 weeks; cough; dyspnoea 3-4 days.	Fairly well nourished, forward for age; febrile; dull left base; flattening; absent breath sounds; aspiration—pus +.	Present on admission.	Pneumococcus P.S.	After initial intrapleural penicillin, rib resection performed; systemic penicillin.
21	8	M	Ill for 1 week; cough and cold; pain in right chest for 2 days.	Well nourished; flushed, febrile; dull to percussion right lower lobe; absent breath sounds; ? fluid; aspiration—nil.	9	Staphylococcus C + aureus P.S.	Penicillin systemically and sulphamezathine by mouth; one intrapleural injection of penicillin.

* P.S. = Penicillin-Sensitive.

APPENDIX B—*continued.*

Progress	Radiograph	Features of case	Result
After repeated aspiration the size of the empyema appeared to be increasing; rib resection.	1: Fluid, left chest. 2: ? Increase in fluid. 3: Drainage proceeding. 4: Chest clear.	No immediate response to repeated aspiration and instillation of penicillin; rib resection performed; no sulphonamides or systemic penicillin given.	Good after rib resection.
Resolution of empyema by aspiration alone; systemic penicillin given; intrapleural × 2.	1: Fluid, right chest. 2: Chest clearing. 3: Chest clear.	Satisfactory response of small empyema to aspiration alone.	Good: no operation necessary.
No true response to sulphonamides or penicillin; when child improved clinically still had signs in chest.	1: Opacity, right upper lobe, ? pneumonia. 2: Opacity still I.S.Q. 3: Chest I.S.Q. 4: Chest I.S.Q.	Although clinical improvement occurred, signs in chest persisted.	Fair: no operation.
No response to sulphonamides; developed empyema after penicillin therapy; no headway with aspiration; resection followed by rapid resolution.	1: Pneumonia left base. 2: Increased density; ? fluid. 3: Resolution proceeding. 4: Chest clearing.	Empyema developed after sulphonamide and penicillin; rapid resolution after resection preceeded by penicillin (intrapleural).	Good with rib resection.
Development of empyema after response of pneumonia to sulphonamide; rapid resolution after intercostal drainage.	1: Pneumonia, left base. 2: ? Fluid, left base. 3: Resolution proceeding. 4: Resolution proceeding.	Rapid response to rib resection after preliminary intrapleural penicillin; no sulphonamides or systemic penicillin given after development of empyema.	Good with rib resection.
Difficulty was experienced in aspirating empyema, ? due to fibrin; rib resection performed—good result.	1: Fluid, left chest. 2: Resolution proceeding. 3: Resolution proceeding.	Good response to rib resection and systemic penicillin.	Good with rib resection.
Pus aspirated once only from chest; response to systemic penicillin good.	1: Opacity, right chest ? fluid. 2: Some clearing of chest. 3: Resolution proceeding. 4: Chest clear.	Good response to systemic penicillin and sulphonamide; small empyema response to one aspiration and instillation of penicillin.	Good; aspiration only (small empyema).

+=Coagulase-Positive.

SUGGESTIONS AND DEMONSTRATION PLANS FOR HOSPITALS FOR SICK CHILDREN*

BY

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The fundamental unit in a hospital is the individual sick person. Any study of a hospital must start from consideration of the needs of the sick individual, and the complexity of a hospital is the result of the many needs of many individuals suffering from a variety of diseases. The children's hospital has three other factors which must be ever present in the minds of the organizers and designers, and which make the task of satisfying all the needs ever more difficult. They are: (1) the prevention of infection from patient to patient and from staff to patient (this aspect alone introducing elements which have a most important effect on the plan); (2) the need for constant supervision of the relatively helpless child; (3) the provision of companionship to counteract home-sickness. These three overriding problems must be faced in the ward unit, and are the crux of the problem in designing hospitals for sick children. The relationship of the ancillary departments to the ward units is, by and large, the same for general as for children's hospitals. The ward unit will, therefore, be considered first and in most detail.

The ward block at the Hospital for Sick Children, Great Ormond Street, London, has been in use for eight years, and there has, therefore, been time for criticism and assessment of the original conception of the ward unit, which represents the attempt to interpret the requirements of the Building Committee in terms of bricks and mortar. Fig. 1 is a plan of a typical ward unit of twenty beds, as at Great Ormond Street; and fig. 2 is a plan of a ward unit such as we would build now, embodying the improvements resulting from our experience in the use of the previous example, and based on the assumption that we might have a better and less congested site on which to build.

Early Wards

Before proceeding with a critical examination of the new ward unit, let us refer for a moment to earlier examples, and eliminate the features which do not subscribe to our programme. Plate IIIa shows a ward built in 1862. Several such wards were built on different floors. After seeing this photograph it is easy to understand that large wards, after the common fashion in adult hospitals of the period, were a step in the right direction.

Plate IIIb shows a large ward of thirty-five beds built in 1880. Some time later ten or fifteen permanent beds were placed on the balcony. The aspect was east and west; the long slits of windows helped to create a large, gloomy, and overbearing ward for children. There was no attempt to prevent cross infection, and no means of controlling any outbreak of infection from spreading to thirty-five patients. A nursing staff of probably six all had to use one room of approximately 80 sq. ft. for disposal of waste, dirty and soiled linen, mackintoshes, storage of specimens, and ward cleaning materials. Open fires radiated as much dust as heat. Treatment had to be at the bedside behind screens.

Plate IIIc shows a ward built ten years later. No appreciable change had taken place, except that the aspect was south, and the ward generally more cheerful. Plate IIId shows a similar ward of 1900, the aspect having reverted to east and west. The hoods to the cots are worthy of notice. There was more light and ventilation, but otherwise the wards remained much the same as before. It would be easy to add many other criticisms of these illustrations, but the herculean work of the staffs of that period produced miracles even under such conditions. In none of these examples was full account taken of all the three factors special to children's wards, especially the prevention of cross infection and the need for constant supervision; though provision was made in all of them for companionship.

Modern Wards

Ward units

Criticism and analysis must now be directed to the more modern experiments in the planning of the ward units, which aimed at much higher standards of hygiene, convenience, and efficiency. Returning to fig. 2, it will be seen that the ward unit is based on twenty beds under the supervision of one sister, subdivided into two sub ward units of ten beds each. Each ten-bed unit is further divided into four single-bed wards and one six-bed ward. The

* Read at the Annual Meeting of the British Paediatric Association, Rugby, August 2, 1946.
† Of Stanley Hall and Easton and Robertson, Architects.

FIG. 1.

Key:

1. 6-Cot Wards.
2. Bathrooms.
3. Sink Rooms.
4. Treatment Rooms.
5. Clinics.
6. Waiting Rooms.
7. Media Preparation.
8. Wash up.
9. Main Laboratory.
10. Bio-chemical Laboratory.
11. Single-cot Wards.
12. Ward Kitchens.
13. Cleaners.
14. Lifts.
15. Medical Ward Sister's Office.
16. Men's Cloaks.
17. Women's Cloaks.
18. Waiting Room for Laboratory Section.
19. Secretary and Records.
20. Bio-chemist.
21. Director.
22. Assistant Pathologist.
23. Technicians.
24. Surgical Ward Sister's Office.

1.	6-bed Ward	484	sq. ft.
2.	Single Bed Ward	99	,, ,,
3.	Nurses' Station	117	,, ,,
4.	Sink Room	117	,, ,,
5.	Treatment Room	195	,, ,,
6.	Patients' Bath	117	,, ,,
7.	Nurses' W.C.		
8.	Patients' W.C.		
9.	Ward Kitchen	117	,, ,,
10.	Demonstration Room	195	,, ,,
11.	Sister's Office	117	,, ,,
12.	Balcony		
13.	Service Lift		
14.	Passenger Lift		
15.	Hall		
16.	Visitors' Waiting	120	,, ,,
17.	Stairs	24	,, ,,
18.	H. M. C.	24	,, ,,
19.	Ward Store	48	,, ,,

Total Area of Ward approximately 4,000 sq. ft.

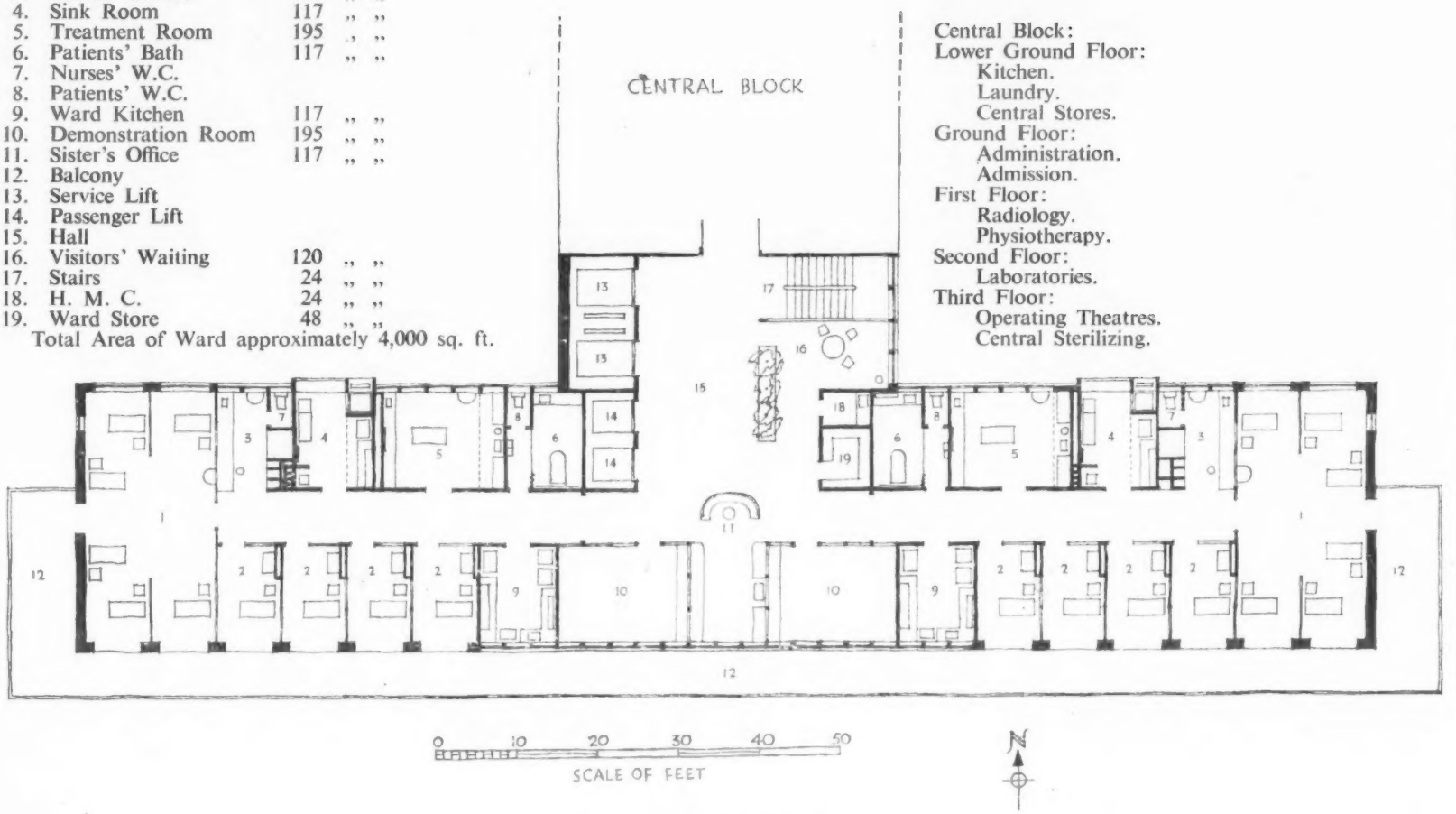

FIG. 2.—Ward Unit, 20 beds.

advantages claimed for this layout are: (1) prevention and control of cross infection; (2) constant supervision, by arranging for all the patients to be seen from the focal points in the units; (3) companionship, by associating patients of similar ages in six-bed wards; (4) isolation of infant, infectious or very ill cases in single-cot wards; (5) special treatments, i.e. iron lung, can be administered without disturbing other patients; (6) a flexible arrangement of patients which allows for the grouping of cases to each consultant; (7) reduction of the scale of rooms, to inspire and induce confidence in children on admission.

The main services and utility rooms are duplicated in each unit. This apparent extravagance can be justified on the following grounds: (1) in the event of an epidemic, any of the sources of cross infection are limited to ten beds: (2) the time spent by the nursing staff in movement between patients is halved, and much additional time can, therefore, be devoted to the supervision and care of patients.

The wards can now be considered in greater detail by examining each of the major rooms.

Fig. 3 shows a single-bed ward, with a south or

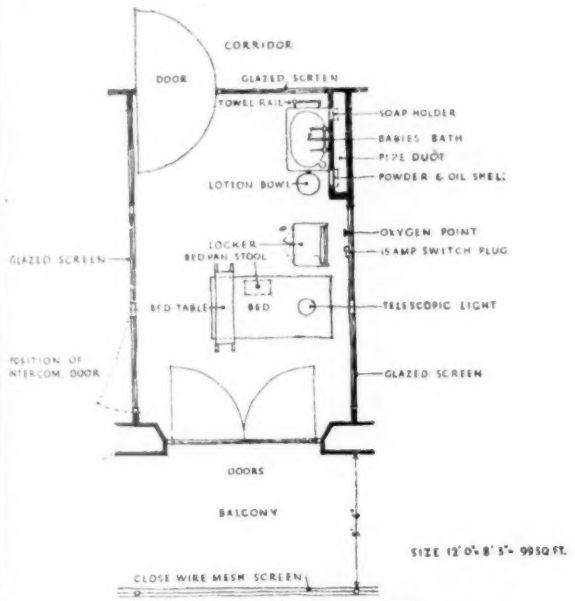

FIG. 3.—Single Cot Ward.

south-east aspect. The bed is arranged so that the patient can be approached from the right-hand side, and examined, nursed, or treated from either. There is sufficient space for a cot or bed for the older child. The area is 99 sq. ft. This is greater than the minimum usually recognized, 70 sq. ft., but is based on the space required round the bed for examination and nursing at the bedside. In sequence from left to right are the following facilities: (a) the surgeon's lavatory, with babies' bath, soap, lotion bowl; powder and oil, and towel rail; (b) a bedside locker, with the patient's towel, mug, tooth brush, toys, clothes, etc.; (c) oxygen point; (d) a 15 amp. power point, for portable x-ray apparatus, cardiograph, or electric fire; (e) a bedpan stool; and (f) a bed table. There will also be the medical record card holder, the nurse's gown, curtains, and chairs. There are windows and cross ventilation; blinds are necessary; and there is a smooth run-out on to the balcony, with no steps. The balcony is 5 ft. 6 in. wide, screened to 6 ft. 6 in. with a close steel mesh. Other points to be noted are: (1) the glazed screens, made of steel, flush to the wall, and cork-filled; and with plate glass, and round, easily cleaned corners; (2) the doors, a minimum of 3 ft. 3 in. wide, on check-action floor springs, with a simple bolt on the outside only, and an ample rubber kicking plate; (3) soft water, mechanical or natural, should be available as an essential requirement at all nursing points; (4) the ward can be cleaned by vacuum; (5) the walls and ceiling are finished with acoustic tiles, the floor with terrazzo; (6) the heating is by a panel in the ceiling; (7) artificial lighting by a multi-purpose telescopic fitting is suggested, the alternative choice being high-intensity fluorescent tubes.

Plate IIIe shows a single-bed ward at the Hospital for Sick Children, Great Ormond Street, and Plate IIIf a surgeon's lavatory, with babies' bath containing a recess for soap, powder, oil and thermometer; the lotion bowl, and towel rail. The lavatory is in fireclay with a surround of tiles, and the fittings fold flat to the wall. For those unfamiliar with what is meant by ' panel heating,' Plate IIIg gives an example of the system as installed at Great Ormond Street.

Plate IIIh shows the six-cot ward, which is designed to run across the full width of each end of the unit, in order to obtain direct cross-ventilation. The patients are partly isolated by glazed partitions 6 ft. 6 in. high. There is direct access to the balcony. Otherwise the services, finishes, etc., are as in the single-cot ward.

Supervision. The second of the special factors affecting the planning of the children's ward is constant supervision. It is important, therefore, that facilities should be arranged in a planned sequence so that the organization and routine of all the aspects of examination, treatment, and nursing can be accomplished with the greatest efficiency. Throughout these plans the left-to-right-hand sequence has been adopted as the basis for the arrangement of fittings and services. The most important services, or those to which there is the most traffic, are placed in the central position relative to the patient, and priority in position is given in turn according to the relative density of movement. The focal point of supervision is the nurses' station (fig. 4). From this position the nurse can see at a glance all the patients in the unit. This space is a ventilated lobby with built-in furniture, open to the corridor, and with a glazed partition to the six-bed ward. The following

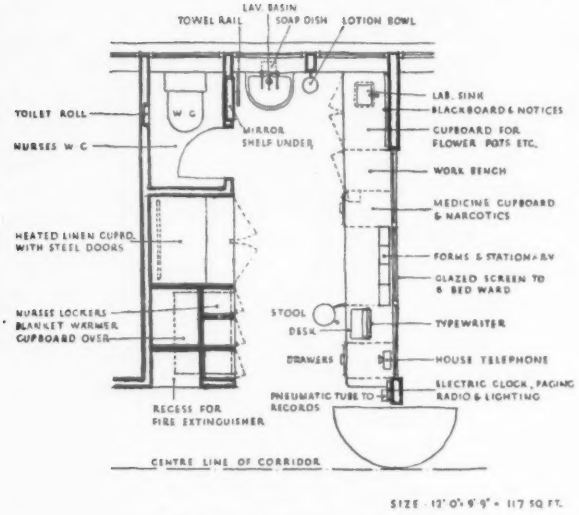

FIG. 4.—Nurses' Station.

facilities are provided: (1) a nurse's locker; (2) a recess for fire apparatus; (3) a blanket-warmer and operation clothes; (4) linen cupboards; (5) a nurse's W.C.; (6) a mirror, lavatory basin, towel rail, soap holder, and lotion bowl; (7) a notice board and blackboard; (8) poisons and narcotics; (9) facilities for the preparation of medicine; (10) a flower bench and laboratory sink, with cupboards underneath for vases, and a waste bin; (11) a writing desk and stationery holder; (12) an electric clock, pageing and lighting switches, radio control, and house telephone; (13) a pneumatic tube to the records department.

Cupboards with steel fronts are used for heated linen, and cupboards throughout should be standard units which can be easily removed for maintenance.

The sink room. Fig. 5 shows the sink room, which has been designed with a dirty side and a clean side. On the left is: (1) an incinerator for burning soiled dressings and waste; (2) a bed-pan washer of the built-in foot-operated type; (3) a porcelain slab and soil sink for washing mackintoshes, and storage racks underneath; and (4) space for a laundry trolley. It should be noted that a hood is placed over the sterilizers, and an extract fan provided to ensure the speedy evacuation of moisture-laden air and a flow of air from the corridor; a fly screen is provided to the window. Bed-pan washers are built-in. Plate IVj shows a bed-pan sterilizer and bed-pan rack. This should be contrasted with a sink room of 1880 (Plate IVk), in which all the utilities for thirty-five patients had to be carried to the one and only household sink.

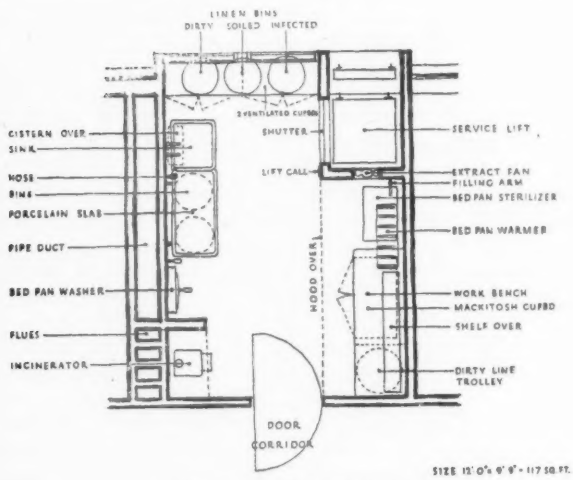

FIG. 5.—Sink Room.

Treatment room. Fig. 6 shows the treatment room designed for the treatment of patients, clinical examinations, and the preparation and storage of medical and surgical supplies. The couch is arranged for right-hand treatment. An instrument panel on the wall is fitted with air pressure (particularly for ear, nose, and throat wards), suction apparatus, oxygen, and a 15 amp. plug. There is a work bench with store cupboards underneath for medical and surgical supplies, dressing drums, etc.; a view box for wet and dry plates; a laboratory bench, with a bunsen sink, and a microscope point with ventilator, and cupboard beneath; a surgeon's lavatory, and the now usual accompaniment of soap holder, lotion bowl and towel rail; and lotion cupboards and hot water bottle store; a water boiler with a fomentation boiler in the top; instrument and bowl sterilizers; and a refrigerator for penicillin and pack ice.

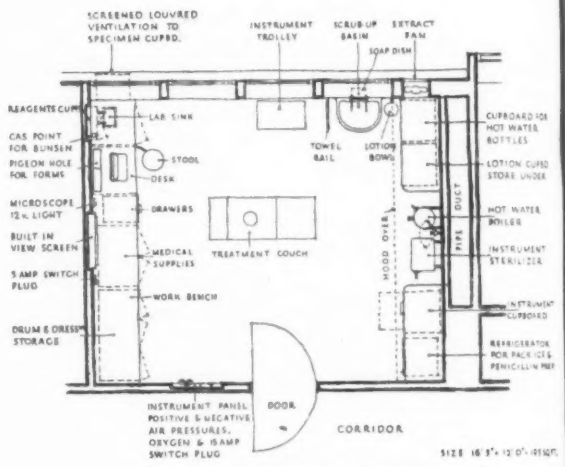

FIG. 6.—Treatment Room.

Plate IVl shows the treatment room at the Hospital for Sick Children, Great Ormond Street. It is too small, but is indicative of the type of fittings to be used. Plate IVm shows the hot water boiler and instrument sterilizer. From our experience at Great Ormond Street the following 'do's' and

'don'ts' in respect of sterilizers have been established: (1) don't have the steam valve under the sterilizer; (2) do have it remote; (3) don't have high pressure for normal ward use; 5 lb. is sufficient; (4) don't have any other fittings under sterilizers; (5) do have hot water filling arms; (6) do have a non-porous and well-drained floor; (7) do have mechanically lifting tray; (8) do arrange for steam to be carried away by mechanical ventilation; (9) do arrange for the valve to the waste to be readily accessible.

Bath room. Fig. 7 shows the patients' bath room

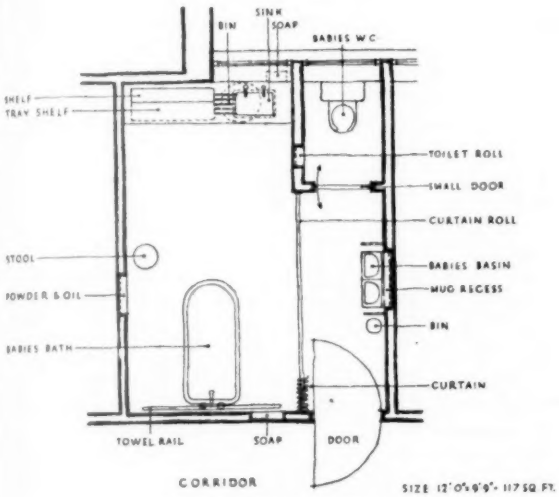

FIG. 7.—Patients' Bath.

and W.C. It is, we believe, a common arrangement for the Sister to be responsible for the washing of the patients' woollies, and facilities for this have been incorporated in this room, which includes a bath, long hot towel rail, nurses' store, powder recess, etc., a work bench with a rack underneath for trays for laying out washing bowls for patients, and a patients' W.C. and lavatory.

Fig. 8 shows the ward kitchen, where the same left-to-right sequence is maintained as kitchen specialists are advocating for domestic purposes, i.e. reception, holding, preparation, delivery: to which we must add sterilization. The ward kitchen is, therefore, laid out as follows: (1) refrigerator; (2) cooker; (3) work bench with a pot rack beneath and a shelf above, and a hot towel rail; (4) a sink with a recess for soap and solvents, and garbage cans beneath (this is the same size as the sink room); (5) a sterilizer for crockery; (6) crockery storage space, with sufficient cutlery for the trays in the drawers under the bench; (7) grocery storage space; (8) a toaster, mincer, and mixer; (9) a tray rack; (10) a notice board, and diet sheets, etc.; (11) a towel rail; and (12) a food trolley. The walls are tiled, the floor terrazzo, and the ceiling painted. There are fly screens to the windows. This plan is based on distribution of food by trolley, and would need modifying if any of the other systems of food distribution were adopted. Plate IVn shows the ward kitchen at Great Ormond Street.

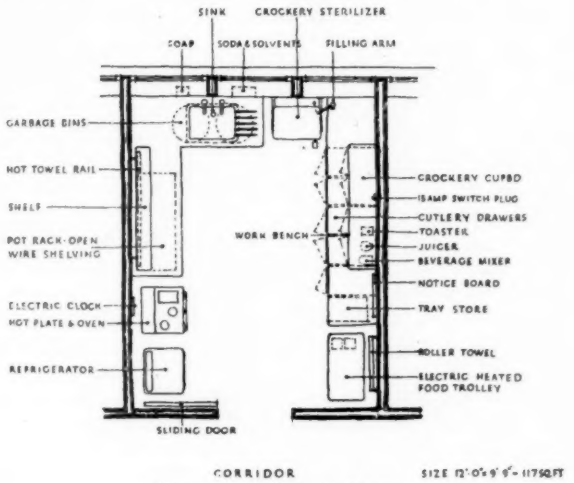

FIG. 8.—Ward Kitchen.

Demonstration room. Referring again to fig. 2, it will be seen that provision is made for a demonstration room designed as a dual-purpose room; this is particularly necessary where post-graduate teaching courses are planned. It is built (1) for teaching, with view screen and wash basin; (2) as a play room, with a south aspect, and plenty of cupboard space for storage of toys. Here children who are not bed-ridden can play under the supervision of the Sister. The Sister's office, with bow window and desk, is the control centre of the two ten-bed wards, from which the entry of staff and all visitors can be supervised. Lining each wall are bulk stock cupboards where linen, stationery and medical and surgical supplies can be kept. An enquiry desk where the Sister can interview parents is kept outside the office. The housemaid's closet and Sister's cupboard are planned in the re-entrant angle. Beside the house telephone, there is an extension from the G.P.O. switchboard to answer outside calls and enquiries about patients.

Visitors' room. The visitors' room forms part of the general circulation space, and should be easy for strangers to identify when they enter the unit for the first time in their usual forlorn state of bewilderment. To most doctors the visitors are an undesirable and unnecessary nuisance; by planning pleasant reception space for visitors it is suggested that much can be done to enhance the prestige of the hospital.

Circulation. With the above arrangement, in an area of 4,000 sq. ft. we can nurse twenty patients and ensure that (1) we have taken action to reduce and control cross infection; (2) all patients will be under constant supervision; and (3) adequate

arrangements have been made for companionship of the older and less ill children. The main limitations of this plan are (1) the points of support are unusual; and (2) the disposition of services is involved. The plan does not readily lend itself to superimposition on other accommodation. These limitations are overcome if the wards are planned vertically. The maximum number of beds, therefore, in any block, is 180, as the heights of buildings are generally controlled to a maximum of 80 ft. A vertical circulation is, of course, dependent on an efficient lift service. The essential point about a lift service is that all the lifts should be concentrated in a central position so as to offer the maximum opportunity for serving callers on different floors. It is also important to arrange for separate lifts for passengers, patients, and service. A device called 'automatic collective intercept control' should be fitted, to overcome the exasperating performance of lifts continually passing the intermediate floors. The bed lifts and service lifts should be interchangeable and capable of manual operation. Lifts should be self-levelling, and the motor rooms and motor supports carefully insulated and treated to prevent transmission of noise throughout the building. Plate IVp gives an idea of the services required for a plan of this type, and shows at once how economical vertical development is achieved. Plate IVq is an external view of the ward blocks at Great Ormond Street, showing a method of expressing the balconies.

Analysis of Accommodation

In order to introduce the problems of piecing together the ancillary, administrative, and mechanical services, an appendix has been added giving schedules of accommodation for each department, together with the relative sizes of each room. The schedules have been correlated, grouped and summarized, to show the total area of the hospital divided by the number of beds for hospitals of various sizes, as follows: a forty-bed hospital, 700 sq. ft.; an eighty-bed hospital, 500 sq. ft.; a hundred and sixty-bed hospital, 460 sq. ft.; a two hundred-bed hospital, 431 sq. ft. It is hoped that they may be of use to those who are intending to build new wards, both in framing requirements and in giving instructions to the architect.

It will be seen from the summaries that the additional 30 sq. ft. per bed in the single-bed wards represents a very small fraction of the total area of hospital per bed; also how relatively extravagant in floor area a small hospital of forty beds is, compared with one of two hundred beds. If plotted, the graph straightens after two hundred beds, and it is doubtful if larger hospitals can effect a saving below the 400 sq. ft. per bed.

Ancillary Departments

It is impossible here to discuss the ancillary departments in the same detail as the wards, and a very brief reference will be made to the major problems, and to any problem peculiar to a children's hospital in these units.

Plate Vr takes us back again to the close of the nineteenth century, and shows an operating theatre of that period. It is a very good one, except that the ancillary rooms are inadequate. Plates Vs and Vt show the theatre at Great Ormond Street, which was planned by the hospital staff with the same open-mindedness and originality used on the ward units. It is probably not important for the theatres to be planned on the top floor. Plate Vu shows the sterilizer room.

Plate Vv shows the kitchens, which are unresolved problems in nearly all hospital plans. The greatest density and volume of inter-department movement takes place between the kitchen and the wards. The former should, therefore, be as central as possible. The choice can usually be narrowed down to a central position in a semi-ground floor or on the top floor. A better kitchen plan and circulation can be designed in the first case where freedom of space allows for difficulties arising from such a complex circulation as in the modern kitchen, e.g. the Hospital for Sick Children. A top-floor kitchen gives the best ventilation and light, both important factors in kitchen design; but the plan is handicapped by the space available for the plans of the departments underneath, for example, Westminster Hospital.

The varied dietetic requirements of many sick children create a different problem from that obtaining in an adult or general hospital. There is the addition of the milk laboratory, and the question arises whether it is economical to cook the bulk food for the staff and nurses in the same kitchen as the many individual preparations for the children, or whether it is best to divide the kitchen staff and have two separate kitchens—one for patients, the other for staff.

Plate Vw shows the laboratories at the Hospital for Sick Children, Great Ormond Street. This is another essential and important department, and a keen competitor for an area in a central position in the plan. If in this article the laboratories, radiology, and physiotherapy departments are not commented on, since there are no difficulties in planning them which are peculiar to children's hospitals, it is not to be inferred that they should not receive the closest attention and study in plan, circulation, and detail.

The out-patients' department, too, is a subject in itself, with a special claim to attention and comment from paediatricians, because the out-patient treatment of children is a different problem from that of similar treatment in a general hospital.

The hospital site, whether in town or country, will have a most important influence on the planning and inter-relationship of the various departments. It is necessary, in selecting a site, to consider: (1) accessibility for patients, visitors, staff, and personnel, and the relation of the site to public transport; (2) accessibility and circulation on the site of traffic and deliveries of supplies, bulk stores,

and fuel; (3) availability of public utilities, such as water, electricity, gas, telephones, and sewage disposal; (4) freedom from nuisances, noise, and noxious businesses; (5) size, availability, and preservation of trees; (6) topography; (7) town planning acts relating the site to the requirements of a local region.

We should like to acknowledge the unfailing interest and many ideas which have been contributed by the physicians, surgeons, nursing and administrative staffs at the Hospital for Sick Children, Great Ormond Street, London, to the planning problems that have been discussed.

APPENDIX

TABLE 1

NURSING SERVICES: AREA DISTRIBUTION

No. of beds	40	80	160	200
Patients' areas (nursing units)	8,008 sq. ft. (2)	16,016 sq. ft. (4)	32,032 sq. ft. (8)	40,040 sq. ft. (10)
Bed areas	3,628	7,256	14,512	18,140
Nurses' station	468 (4)	936 (8)	1,872 (16)	2,340 (20)
Sick room	468 (4)	936 (8)	1,872 (16)	2,340 (20)
Treatment room	792 (4)	1,584 (8)	3,168 (16)	3,960 (20)
Bathrooms and Patients' W.Cs.	468 (4)	936 (8)	1,872 (16)	2,340 (20)
Ward kitchen	468 (4)	936 (8)	1,872 (16)	2,340 (20)
Demonstration room	792 (4)	1,584 (8)	3,168 (16)	3,960 (20)
Sister's office	468 (4)	936 (8)	1,872 (16)	2,340 (20)
Visitors	288 (2)	576 (4)	1,152 (8)	1,440 (10)
H.M.C.	56 (2)	112 (4)	224 (8)	280 (10)
Stores	112 (2)	224 (4)	448 (8)	560 (10)
Total	8,008	16,016	32,032	40,040

(*continued on next page*)

TABLE 2
NURSING SERVICES (continued): AREA DISTRIBUTION

No. of beds	40	80	160	200
Operating suite	1,775 sq. ft.	2,855 sq. ft.	3,640 sq. ft.	4,205 sq. ft.
Major operating theatres	310 (1)	620 (2)	930 (3)	1,240 (4)
Minor operating theatres	260	225	225	225
Cystoscopic room	—	150	150	150
Local sterilizing rooms	100 (1)	100 (1)	200 (2)	200 (2)
Scrub-up room	50 (1)	90 (2)	100 (2)	130 (3)
Central sterilizer rooms	400	520	640	750
Instrument room	—	—	100	120
Utility room	125	125	125	125
Cleaners	20	20	20	20
Sister's office	—	75	100	120
Doctors' lockers and changing room	240	300	350	350
Nurses' lockers and changing room	160	160	220	280
Laboratory	—	50	50	50
X-ray and dark room	—	130	130	130
Plaster room	—	130	130	130
Splint store	—	50	60	75
Anaesthetic equipment store	110	110	110	110
Total	1,775	2,855	3,640	4,205

TABLE 3
NURSING SERVICES (continued): AREA DISTRIBUTION

No. of beds	40	80	160	200
Admission	665 sq. ft.	730 sq. ft.	810 sq. ft.	830 sq. ft.
Admission room	275	275	275	275
Observation room	200	200	200	200
Office and waiting room	—	70	70	70
Bathroom	60	60	60	60
Lavatories and W.Cs.	20	20	20	20
Utility	—	—	70	70
Storage	65	70	80	100
Stretchers and trolleys	35	35	35	35
Total	655	730	810	830

TABLE 4
ANCILLARY SERVICES: AREA DISTRIBUTION*

No. of beds	40	80	160	200
Pathology	620 sq. ft.	940 sq. ft.	1,260 sq. ft.	1,580 sq. ft.
Laboratory	250	400	525	650
Mortuary (including refrigeration storage)	250	300	325	350
Office	100	120	150	200
Waiting room	—	100	100	120
Lavatories and W.Cs.	20	20	40	60
Chapel	—	—	120	200
Total	620	940	1,260	1,580
Radiology	400 sq. ft.	600 sq. ft.	850 sq. ft.	1,200 sq. ft.
Physiotherapy	160 sq. ft.	180 sq. ft.	200 sq. ft.	250 sq. ft.
Pharmacy (bulk pharmacy storage included in central stores area)	185 sq. ft.	380 sq. ft.	555 sq. ft.	645 sq. ft.
Pharmacy	185	260	260	260
Solution room	—	120	120	120
	—	—	175	265
Total	185	380	555	645

* No area has been given for specific research departments.

TABLE 5
ADMINISTRATION SERVICES: AREA DISTRIBUTION

No. of beds	40	80	160	200
Administration	1,875 sq. ft.	2,635 sq. ft.	3,150 sq. ft.	3,760 sq. ft.
Main lobby and waiting room	320	420	520	620
Public lavatories	90	90	90	120
Telephones	10	10	15	15
House physician	150	150	150	150
Social service	—	160	200	250
Information and telephone	90	100	100	130
Superintendent	160	200	200	250
Secretary	125	125	125	125
Business offices	250	440	630	780
Staff lavatories	90	90	90	90
Record room	200	260	320	320
Matron's office(s)	140	160	260	320
Staff common room	250	250	250	300
Library and conference room	—	180	200	220
Total	1,875	2,635	3,150	3,760
Staff facilities	580 sq. ft.	940 sq. ft.	1,320 sq. ft.	1,660 sq. ft.
Nurses' locker room	320	500	680	860
Porters' locker room	130	220	320	400
Female staff	130	220	320	400
Total	580	940	1,320	1,660
Storage	2,175	4,300	5,500	6,300
Record storage	175	300	500	800
*Central lines	2,000	4,000	5,000	5,500
Total	2,175	4,300	5,500	6,300

* This does not include bulk fuel storage.

TABLE 6
SERVICE DEPARTMENTS: AREA DISTRIBUTION

No. of beds	40	80	160	200
Kitchens	2,800 sq. ft.	3,760 sq. ft.	5,175 sq. ft.	6,000 sq. ft.
Main kitchen and preparing room	1,500	1,800	2,500	2,750
Diet kitchen and office	140	200	230	260
Milk preparation and milk stores	130	150	175	200
Dishwashing	120	170	200	250
Refrigeration:				
Meat	30	30	30	35
Dairy	30	30	45	45
Fruit and vegetables	30	30	45	60
Larder stores	100	150	200	250
Garbage and can ward	70	100	150	200
Dining rooms, staff	400	700	1,000	1,200
Dining rooms, employees	250	400	600	750
Total	2,800 sq. ft.	3,760 sq. ft.	5,175 sq. ft.	6,000 sq. ft.
Housekeeper's Department	1,250 sq. ft.	2,090 sq. ft.	2,550 sq. ft.	3,070 sq. ft.
Housekeeper's office	110	140	150	170
Central linen room (sewing room included)	200	250	300	350
Soiled linen (including disinfecting chamber)	140	200	300	350
Laundry	800	1,500	1,800	2,200
Total	1,250 sq. ft.	2,090 sq. ft.	2,550 sq. ft.	3,070 sq. ft.
Mechanical Department (no fuel storage included	1,180 sq. ft.	1,650 sq. ft.	1,950 sq. ft.	2,220 sq. ft.
Boiler House and pump room	900	1,200	1,400	1,500
Electrical intake	80	120	150	200
Engineer's office	—	80	100	120
Works	200	250	300	400
Total	1,180	1,650	1,950	2,220

TABLE 7
CIRCULATION SPACE

No. of beds	40	80	160	200
Circulation space*	5,770 sq. ft.	9,630 sq. ft.	13,820 sq. ft.	15,640 sq. ft.
Corridors	4,450	7,550	10,700	11,740
Lifts	240	640	960	1,200
Stairs	1,080	1,440	2,160	2,700
Total	5,770	9,630	13,820	15,640

* These figures are approximate only and are based on two stories and lower ground floor for forty beds; 4 stories and lower ground floor for eighty beds; eight stories and lower ground floor for one hundred and sixty beds; eight stories and lower ground floor for two hundred beds.

TABLE 8

AREA AND PERCENTAGE AREA DISTRIBUTION

No. of beds	40 Area sq. ft.	80 Area sq. ft.	160 Area sq. ft.	200 Area sq. ft.
Nursing Services :				
Patients' areas	8,008	16,016	32,032	40,040
Operating suite	2,775	2,855	3,640	4,205
Administration	665	730	810	830
Total	10,438	19,601	36,482	45,075
Ancillary Departments :				
Pathology	620	940	1,260	1,580
Radiology	400	600	850	1,200
Physiotherapy	160	180	200	250
Pharmacy	185	380	555	645
Total	1,365	2,100	2,865	3,675
Administration Services :				
Administration	1,875	2,635	3,150	3,760
Staff facilities	580	940	1,320	1,660
Storage	2,175	4,300	5,500	6,300
Total	4,630	7,875	9,970	11,720
Service Departments :				
Kitchen	2,800	3,760	5,175	6,000
Housekeeper's department	1,250	2,090	2,550	3,070
Mechanical department	1,180	1,650	1,950	2,220
Total	5,230	7,500	9,675	11,290
Circulation area	5,770	9,680	13,820	15,640
Total hospital area	27,744	44,626	70,930	86,220
Area per bed	685	583	455	437

DEPARTMENTS AND SERVICES NOT INCLUDED IN ANALYSIS

1. Out-Patients' and ancillary departments.
2. Doctors' private consulting rooms.
3. Research departments.
4. Students' accommodation.
5. Bath fuel stores.
6. Garages.
7. Resident doctors' quarters.
8. Nurses' home and nurses' training school.
9. Staff home.
10. Matron's quarters.

DYSONTOGENETIC PITUITARY CYSTS
(PITUITARY CACHEXIA IN CHILDHOOD)

BY

H. S. BAAR, M.D.

(From The Children's Hospital, Birmingham)

The confused classification of pituitary tumours was clarified at the beginning of this century by the work of Erdheim (1904, 1926). In a series of exemplary papers, he gave proofs that a variety of solid and cystic tumours of the pituitary gland and its stalk have a common origin in the displaced stratified squamous epithelium of the hypophyseal duct. This histogenesis is well expressed in the designation ' hypophyseal duct tumours ' (Erdheim) or craniopharyngeomata. Recently Ingraham and Scott (1946) rightly objected to the term craniopharyngeoma, pointing out that the hypophyseal duct develops from the ectodermal stomodeum and not from the entodermal primitive pharynx. They suggested tentatively the term ' craniostomodeoma.' The designation ' craniopharyngeoma ' however, being in common use, will be retained in this paper. While the experimental work on the pituitary has made spectacular progress, very little has been added since Erdheim's classical monograph (1926) to our knowledge of the morphogenesis of pituitary tumours. Unfortunately much confusion has been caused by the use of such names as ' tumours of Rathke's pouch,' ' cysts of Rathke's pouch,' ' adamantinomata of the pituitary,' etc. The use of the term ' tumour of Rathke's pouch ' as synonymous with craniopharyngeoma is particularly deplorable, as will be obvious by reference to the developmental relationship of Rathke's pouch and its cavity to various parts of the pituitary gland. This shows that Rathke's pouch is at first a rather flat bag which, after frontal turning of the lateral and later cranial seams, resembles a basket. In the frontal wall of the basket a midsagittal crest is then formed, which in cross section appears as a solid process. By proliferation of the crest and of the lateral (frontally turned over) seams, a large number of solid glandular columns and narrow tubules are produced, which, with the invaded vascular connective tissue, form the main mass of the adenohypophysis. The upper seam with a few wider tubules probably gives rise to the pars tubularis and some of the cysts of the medullary zone (Hochstetter, 1924; Benda, 1932; Guizetti, 1933). After obliteration of the craniopharyngeal duct, the original cavity of Rathke's pouch is represented in embryonic life by the ' primary Rathke's cyst,' which in young infants still persists in the form of Rathke's cleft (Koelliker's space = Frazer's pituitary lake, Frazer, 1921). By progressive segregation from the cleft, which was originally single, small colloid cysts are formed in the medullary or intermediate zone of the pituitary; these Kraus (1926) calls ' secondary Rathke's cysts.' However, the cysts of the medullary zone, which latter is often erroneously called ' pars intermedia,' only in part originate from the segregation and partial obliteration of Rathke's cleft; some are the product of cellular degeneration, and others probably arise from hollow glandular buds of the cranial seam of the pituitary basket (Collin, 1923; Benda, 1932; Berblinger, 1932; Guizzetti, 1933; Selye, 1943). Usually the origin of the cysts is not recognizable from their morphology. Bailey (1932) says that cysts deriving from Rathke's cleft may be distinguished from other cavities in this region by their being lined by ciliated epithelium; this statement is misleading, because an intact Rathke's cleft is often seen in young infants, where ciliated epithelium is found only occasionally and in limited areas. Cysts lined by ciliated epithelium are, except for the suprasellar ones, certainly derived from the original Rathke's cyst, but the majority of colloid cysts, produced by the segregation of Rathke's cleft, are lined by cubical and not by ciliated epithelium.

The craniopharyngeal duct is pulled upwards anteriorly during the proliferation of the anterior wall of Rathke's pouch, and in the rare cases of persisting craniopharyngeal duct the cranial end of the intrasphenoid canal is situated in the anterior part of the sella, in front of the eminentia olivaris. ' The region of the insertion of the erstwhile hypophyseal duct is carried upwards, by the . . . rotation of the developing gland, to the anterior infundibular and upper pars anterior surfaces ' (Duffy, 1920). How far upwards the insertion of

the craniopharyngeal duct, which is originally situated at the caudal end of the pouch, can be carried by the developing glandular mass is well seen in a figure of Hochstetter's, where a persisting rest of the hypophyseal duct is seen inserted high (i.e. cranially) on the ventral aspect of the adenohypophysis. This explains the main localization of displaced squamous epithelium on the anterior aspect of the pituitary, and especially of its stalk and the corresponding situations of craniopharyngeomata. Schematic drawings and reproductions of wax models illustrating the developmental anatomy of the pituitary may be found in papers of Mihálkovics (1875), Hochstetter (1924), Erdheim (1926) and Benda (1932). The whole anterior lobe of the pituitary being derived from the wall of Rathke's pouch, the designation ' tumours of Rathke's pouch ' could, in fact, be applied with more justification to adenomata of the pituitary than to craniopharyngeomata, which are derived from displaced squamous epithelium of the craniopharyngeal duct, which in embryos of 12 to 16 mm. crown-rump length is already well differentiated from Rathke's pouch proper. If, on the other hand, the term ' Rathke's pouch ' is used as synonymous with ' primary Rathke's cyst,' which is done by Worster-Drought et al. (1927) the designation ' cysts and tumours of Rathke's pouch ' can be applied only to those arising from the pituitary cleft and its lining epithelium, and not to the vast majority of craniopharyngeomata. The term ' tumour of Rathke's pouch ' thus leads to confusion of craniopharyngeomata with cysts (either colloid or ciliated epithelial) which develop from the primary or secondary Rathke's cysts and which have histogenetically nothing in common with the former. Frazier and Alpers (1934), who do not agree with the present classification of pituitary tumours, proposed a classification into (1) adenomata, (2) tumours of the pituitary stalk, and (3) tumours of Rathke's cleft. Except for the adenomata, this classification is purely topographical, makes no distinction between neoplastic and non-neoplastic cysts, and cannot be considered as satisfactory when a morphogenetic classification is possible.

It is hoped that the publication of the two following cases may contribute to a more satisfactory classification of pituitary cysts. Moreover the cases present several other points of interest. In the first place they are examples of the very rare pituitary cachexia in young children. The few cases of Simmonds' disease in childhood (Thomas, 1933; Goebel, 1932; Geldrich, 1939; and others) were almost all only clinically observed. Only one case (Simmonds, 1916) is mentioned in Graubner's (1925) review and Escamillo and Lisser (1942), reviewing all cases of pituitary cachexia, found among 111 cases verified by autopsy, only one case under ten years. Secondly, it is exceptional for even large colloid cysts, such as those described in this paper, to cause clinical symptoms. Goldzieher (1913) described a large colloid cyst causing diabetes insipidus, and Kiyono (1926) a case of pituitary cachexia due to similar cyst.* Merz (1930) described a case of pituitary cachexia due to a pea-sized colloid cyst between the anterior and posterior lobes, but the presence of sclerotic changes at the insertion of the pituitary stalk makes the interpretation of his case somewhat uncertain. Finally, in one patient described in the present paper, the pituitary cyst was associated with syringomyelia, and in the other with fibrocystic dystrophy of the pancreas. While the first association can be regarded as a simultaneous occurrence of two developmental disturbances, the possibility of a causal connexion between pituitary and pancreatic disease cannot be ruled out and will be discussed below.

Case 1

After seven months' gestation, a boy was born on March 15, 1941; he was admitted to the Children's Hospital, Birmingham, on July 20, 1945. The child thrived normally until the age of eight months, when he developed pneumonia, for which he was in hospital for several months. Before this he could stand and walk with assistance. A few weeks after his discharge he showed so little improvement that he was readmitted. He remained in hospital until the age of two and a half years. He always had a cough, variable in severity, and a poor appetite. He had no difficulty in swallowing, but the act often produced coughing, which in its turn caused vomiting; he never vomited except after cough. He drank well. He could not sit up by himself, but was able to feed himself when he felt strong enough. He liked to play with an engine, and he would look at a picture book for hours and was not destructive. At the time of his discharge from hospital he was not able to talk much, but uttered words such as ' gee gee.' His sleep was restless. He had no fits. Bowel and urinary functions were good, but if he had been vomiting during the day he had nocturnal enuresis.

Findings on admission. He was an emaciated child who did not smile. He knew the names of a few common objects, but the speech was confined to single words. He seemed to want to rouse himself, but could not succeed. He kept his head on one side, being unable to hold it up, and he sat only with support. There was some nystagmus in all directions, and ? fibrillation of the tongue. There was frequent, unexplosive cough, the chest was full of bronchial sounds, the abdomen normal,

* The paper of Jedlička (*Sborn. lík.*, 1924, 25, 149) describing an apparently similar case was unfortunately not available.

all reflexes brisk, and the voice monotonous. On July 21, 1945, the tongue protruded with difficulty and there was fibrillation, though there was none in the hands, nor any wasting of small muscle groups. On July 22 he regurgitiated through the nose, and the next day he was weaker and the temperature, pulse, and respiration rates were raised and the colour poor. He died on July 24, 1945, and necropsy was performed nine hours after death.

Post-mortem findings. The body was of an extremely emaciated, pale boy. It measured 87·5 cm. long (normal average, 102 cm.). The sitting height was 50 cm. (normal, 56 cm.), and the length of the leg from the anterior superior iliac spine to the internal malleolus was 42·5 cm. (normal, 47·5 cm.). (The normal figures for body length are taken from Kornfeld, 1929; and other measurements from Brock, 1932; and the weights of normal organs in childhood from Copolletta and Wolbach, 1933.)

The thyroid and parathyroid glands appeared normal to the naked eye. The thymus was grossly atrophic. There were extensive and firm adhesions between the pulmonary pleura over the right lung and the costal pleura, and some fibrinous exudate over the lower lobe of the left lung. Moderately dilated bronchi, filled with pus, were seen on the cut surface of both lungs. In the lower lobe of the left lung there were numerous areas of consolidation, brownish-red in colour; there were areas of collapse in the right lung. The tracheo-bronchial lymph nodes were markedly enlarged, soft and hyperaemic. The largest was at the bifurcation and was almost as large as a walnut. The pericardium was normal. The liver was moderately congested. The testicles, each about the size of a pea, were in the inguinal canals.

The sella turcica was normal in sagittal and frontal diameters. The pituitary appeared (on inspection after an incision into the diaphragm sellae) to be replaced by a large pea-sized, thin-walled cyst which apparently filled the whole sella. It was not dissected immediately, but the whole body of the sphenoid bone was removed, fixed in formol saline, decalcified, and dissected in the mid-saggital plane, one half being embedded in paraffin and the other saved. The spinal cord was saved but not dissected immediately.

The costo-chondral junctions were normal on naked-eye examination. The bone marrow of the right femur was dark red throughout.

Histological findings

PITUITARY. There was considerable shrinkage of the pituitary affecting mainly the cyst, which had an antero-posterior diameter of 3 mm. The anterior lobe was reduced to a narrow band which on sagittal section had the shape of a sickle. The pointed end of the sickle was at the floor of the sella turcica, and the diameter increased gradually and reached its maximum of 1·2 mm. at the antero-superior aspect of the cyst. The posterior lobe had a maximal diameter of 1·5 mm. The cyst was situated between the two lobes of the pituitary and extended downwards to the periostium of the sella. (Fig. 1, and Plate Ia.) It was filled with a homogenous material, which appeared pale pink in

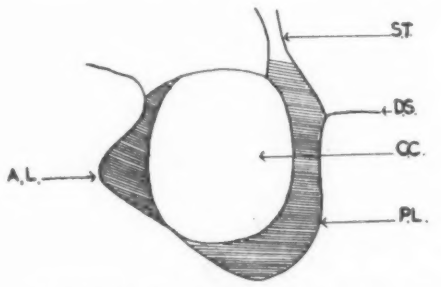

FIG. 1.—Schematic reconstruction of the immediate post-mortem findings on the pituitary in case 1. A.L.=anterior lobe; C.C.=colloid cyst; P.L.=posterior lobe; D.S.=dorsum sellae; S.T.=stalk.

haematoxyline-eosin-stained sections and pale bluish in trichrome stain, and which showed fuchsinophil, fuchsinophobe, and tannin-fast areas by Kraus' (1914) colloid stain. The lining of the cyst consisted of a single, in a few places double, layer of flat or cubical cells which did not show any granulation in their cytoplasm (Plate Ib). Their nuclei were dark, oval or spherical, their cytoplasm pale and amphophil. A few small colloid cysts were also seen along the anterior aspect of the posterior lobe. Here, and occasionally on the posterior aspect, several glands were seen which had the appearance of salivary glands. Such glands are not uncommon in pituitaries. Erdheim (1903) considered them as identical with salivary glands. The structure of the posterior lobe was normal. In the anterior lobe the cells were arranged in parallel, longitudinal strands, instead of the normal tortuous columns, as if compressed between the bone and the cyst. The sinusoids between the cellular strands, however, were wide and engorged, thus suggesting that the cellular disarrangement was due to a chronic pressure directing the growth of the gland and not to an immediate mechanical effect. The numerical relationship between the acidophil and basophil cells was approximately normal. The chromophobe cells were rather scanty. There was no follicle formation in the anterior lobe, and nowhere within this part was there any evidence of colloid degeneration.

THYROID. The vesicles of the thyroid were normal in size; they were lined by cuboid or columnar epithelium. Colloid, which was present in a few vesicles only, showed a pale eosin stain and had in some places a vacuolated appearance. Desquamated epithelial cells were seen in many vesicles.

PARATHYROID. Only one parathyroid gland was examined. It measured 1·7 by 0·7 mm. There

were fairly large areas of fat tissue between the cells, which had all the character of water-clear ' chief cells ' (Plate Ic). Normally no fat cells are seen in the interstitial tissue of the parathyroids before the fifth year of life (Erdheim, 1903).

SUPRARENALS. When the suprarenal glands were examined, only the cells of the zona glomerulosa showed an approximately normal foamy appearance. The cells of the zona fasiculata and reticularis were swollen, their cytoplasm was slightly granular, and pale pinkish in haematoxylineosin stained sections.

The seminiferous tubules of the testis were narrow, lined by one to three layers of cubical or columnar cells with dark nuclei, and separated by broad strands of interstitial tissue. The latter was cellular with numerous fibroblasts in some areas, acellular with broad collagenous fibres in others. Interstitial cells of Leydig were seen only occasionally (Plate Id).

THE MEDULLA. This showed an increased amount of glia at the floor of the fourth ventricle, and specially in the region of the hypoglossal nuclei. There was marked rarefaction, chromatolysis of nerve cells, and ' fading away ' of nerve cells with formation of ghost cells.

THE LUMBAR CORD. The lumbar cord showed the central canal replaced by a cavity 5½ by 3 mm. in diameter in its widest part. The cavity contained some disintegrated nerve tissue. Small parts of its circumference were lined by a single layer of cuboid or columnar cells in epithelial arrangement, the cells with very few exceptions not being ciliated. There was a ring of fibrillary glia, about 0·3 mm. in diameter, surrounding the cavity (Plate Ie and f). The glia fibres were in loose arrangement, but here and there formed patches of dense network. The astrocytes were poorly impregnated by the Cajal method; their processes were irregular and occasionally fragmented. Except for a slight increase of the glia around the central canal, the dorsal and cervical cord showed no pathological changes.

RIBS. The proliferation zone proper of the cartilage was very poorly developed, in many places scarcely recognizable as such. The columnar zone was normal in width, but in numerous places whole columns had undergone severe degenerative changes and the cells had fused with the ground substance of the cartilage. The provisional zone of calcification was interrupted in a few places, and in these it consisted of small isolated patches of calcified ground substance. In several places the osteoid seams of the bone trabeculae were definitely broader than normal. (Completely decalcified ribs, and ribs partially decalcified by Mueller's solution, were examined.)

BONE MARROW. In the rib there was a very cellular bone marrow with numerous normoblasts and myelocytes. In the distal end of the femur there was fat marrow.

Summary of Findings. A four-year-old boy who suffered from his eighth month of life from indefinite symptoms of retarded development, muscular weakness, loss of appetite, and wasting, died with symptoms suggestive of bulbar palsy. Necropsy revealed a large colloid cyst of the pituitary causing a severe atrophy of the anterior lobe. This was associated with syringomyelia of the lumbar cord and a mild gliosis and rarefaction in the region of the hypoglossal nuclei. At the time of death he was 14·5 cm. shorter than the average for his age. His body length was 86 per cent. and the length of the lower limbs 89 per cent. of the normal figure. He may, therefore, be considered as of normal proportion. There was a lipomatosis of a parathyroid, an incomplete descent of testicles with atrophy and interstitial fibrosis of the latter. In addition there was a chronic ulcero-necrotic bronchitis, peribronchitis, bronchiectasis, and adhesive pleurisy.

Case 2

A girl of eight years of age was well until April, 1945, when she started to have eight or nine very offensive, loose, yellow stools daily. She lost her appetite. She had an attack of diarrhoea twelve months before admission, but recovered in three or four days. On admission on July 17, 1945, she was very emaciated, and talked with a slow, monotonous voice; her feet were pale and cold, and there was excessive muscular wasting in her legs. There was slight oedema, and a purpuric rash. On the knees were depressed scales about the size of the head of a pin, surrounded by narrow rings of erythema. There was latent tetany, but no other relevant findings. A five days' collection of stools showed a daily output of 18·4 g. of fat. The total fat was 43·2 per cent. of the dried faeces, and the neutral fat 15·8 per cent. The blood urea was 29 mg. per 100 c.cm., the albumin 1·77 g., and the globulin 1·15 g. There was 248 mg. sodium per 100 c.cm. serum, 477 mg. chlorine (calculated as sodium chloride), 1·0 mg. pyruvic acid, 6·0 mg. calcium, 4·4 mg. phosphorus, and 8·5 mg. inorganic phosphorus liberated in three hours, at 37° C. The water-elimination test for Addison's disease was inconclusive. The test of Robinson et al. (1941) was performed on Aug. 12 and 13, and the resulting quotient was 5·7 (normal more than 25). Another estimation of faecal fat in the period from Aug. 9 to 14 showed a daily output of 24·8 g., with the total fat forming 52·3 per cent. and the neutral fat 18·0 per cent. of the dried faeces.

The blood findings are shown in the table and in the Price Jones curve (fig. 2). The mean corpuscular volume was 81·6 to 85·2 μ^3. The bleeding time was one and a half minutes and the clotting time three minutes (Aug. 17, 1945). An oral and an intravenous glucose tolerance curve showed no gross abnormality. Two units of insulin injected intravenously caused a depression of the blood-sugar level from the fasting level of 104 mg. per 100 c.cm. to 42 mg. per 100 c.cm. after twenty-three minutes. and after sixty-two minutes it was 62 mg. per

100 c.cm. The Mantoux test was negative with 0·1 and with 1 mg. tuberculin. The child was given plasma intravenously, calcium chloride by mouth, and, from Aug. 18, 5 mg. percortin daily. There was a transient improvement after the percortin treatment, but after this a rapid deterioration, and the child died on Sept. 20, 1945. Her weight was

FIG. 2.—Price Jones curve of case 2.

3 st. 11 lb. one week after the onset of the disease, and 1 st. 10 lb. 14 oz. two days before death.

Post-Mortem findings. The body, which was of an extremely emaciated girl, measured 116 cm. long (average, 123 cm.). The distance from the acromion to the tip of the middle fingers was 50 cm. (normal, 53·5 cm.); and from the spina iliaca anterior to the malleous externus, 56·25 cm. (normal, 62·5 cm.). The skin was pale, with a greyish-yellow tinge. Ecchymoses, pin-head to millet-sized, occasionally lentil-sized, and not sharply demarcated, were situated mainly on the anterior aspect of the chest; but there were a few on the anterior abdominal wall and on the limbs, a single one 11 by 5 mm. in diameter on the interior aspect of the lower third of the left thigh, and another measuring 10 by 5 mm. on the radial side of the back of left hand, between the metacarpes of the thumb and the second finger. There were no pubic and axillary hairs. The subcutaneous fat tissue was almost absent, being reduced to small patches, saffron yellow in colour. The bone marrow of the sternum was a dark raspberry red. The tongue showed atrophy of the filiform papillae and several blackish-grey patches approximately in the middle. The right lobe of the thyroid measured 30 by 12 by 9 mm., the left 28 by 9 by 6 mm., the cut surface being moist, granular, and lustrous yellowish pink.

The thymus was grossly atrophic. The heart measured 8·2 by 7·5 by 3·6 cm., and weighed 67 g. (empty) (normal, 80 to 130 g.). The wall of the left ventricle was 9 mm. and that of the right 2 mm. thick. The heart muscle was pale, flabby, and friable. The valves and the septa were normal. The ductus arteriosus was obliterated, and a shallow pit on the aortic side was noticeable.

There was one pinhead-sized subserous haemorrhage on the anterior aspect of the stomach near the greater curvature. Very little fat was present in the great omentum and in the appendices epiploicae. The anus was rather wide; the blood vessels of the mesentery somewhat distended and engorged. The stomach was distended and contained about a handful of a greyish material of the consistency of porridge. Its mucous membrane was normal. The contents of the duodenum were bile-stained, and bile was easily expressed from the gall bladder by manual pressure. The small intestine was collapsed, and the large intestine, especially the pelvic colon, considerably distended. The contents of the small intestine were green, liquid, and somewhat slimy. The large intestine contained watery-green faeces. The mucous membrane of the intestine was normal, and the lymphatic apparatus rather atrophic. The mesenteric lymph nodes were lentil to pea-sized, greyish-white, and normal in consistency.

The liver weighed 1 lb. and showed fatty changes and some congestion. The bile ducts were patent. The pancreas weighed 34 g. and was rather firm, its cut surface being normal in appearance. The spleen measured 6·5 by 4·5 by 1·5 cm. and weighed 27 g. (normal, 69 g.). The capsule was smooth, the colour pale salmon red, and the consistency normal. On the cut surface the Malpighian bodies were fairly large, and the pulp bright red and not diffluent. The right adrenal weighed 3·3 g., and the left 3·5.; their cortex was greyish and poor in lipoids. The left kidney measured 7 by 4·5 by 3 cm. and weighed 59 g. (normal, 75 g.); the right

TABLE

Date	Hb. g. per c.cm. of blood	Erythrocytes (million)	Colour Index	Reticulocytes %	Leucocytes	Platelets	Neutrophil band %	Neutrophil sgm. %	Eosinophils %	Monocytes %	Lymphocytes %
July 23	9·3	?3·6	?0·88	1·8	6,250	290,000	2·0	44·5	0·0	6·0	47·5
Aug. 17	9·6	2·78	1·22	3·4	3,900	222,000	2·0	42·0	3·0	3·0	50·0
Aug. 23	9·8	2·98	1·18	6·6	6,000	307,000	1·0	57·0	1·0	5·0	36·0
Sept. 6	10·8	2·58	1·52	0·8	11,250	337,000	3·0	84·0	0·0	1·0	12·0

measured 8 by 4·5 by 3·5 cm., and weighed 61 g. (normal, 74 g.). Their capsules were easily stripped off, and the surface was smooth and pale yellowish-red. On the cut surface the medulla was dark red; the normal markings of the cortex were indistinct. The renal pelves appeared normal. The right ovary weighed 0·71 g., the left 0·66 g., and they appeared normal.

The vault of the skull showed on both sides of the sagittal suture, close to the coronary suture, triangle-shaped, thin, white, transparent, non-flexible areas. In other areas dark red bone marrow was visible in transmitted light. The thickness of the vault was between 1 and 2 mm. The appearance of the internal aspect was normal. The distance between the anterior clinoid processes was 24 mm., that between the posterior 16 mm. The pituitary appeared normal from above, but when it was removed from the sella a thin-walled cyst, 8 by 8 by 3 mm. with clear, yellowish, apparently gelatinous contents was found replacing a considerable part of its anterior lobe. The size of the whole pituitary was 11 by 8 by 3 mm., its weight being 0·341 g. The depth of the sella turcica was 7 mm. and its midsagittal diameter 9 mm.

The pineal gland measured 14 by 8 by 2 mm. and appeared normal. The labia majora were scarcely discernible, the clithoris rather small, and the vagina and uterus normal. On the sixth left rib the proliferation zone of the cartilage was 2 mm. in depth, and the provisional calcification zone was straight, sharply defined, and about 0·25 mm. in width.

The femur was easily sawn through. Its cortex and the trabeculae of the cancellous bone were thin. The epiphyses were ossified, leaving a narrow epiphyseal cartilage. The bone marrow of the proximal three quarters of the femur was raspberry-red and that of the distal quarter was pale, greyish-white, and gelatinous. The marrow of the proximal epiphysis was red, and that of the distal epiphysis pale greyish-white.

Histological findings

PITUITARY. The Rathke's cleft was very considerably dilated, and, on midsagittal section, triangle-shaped. It contained a large amount of fuchsinophobe colloid with a small admixture of fuchsinophil and tanninfast colloid. The wall of the cyst was ruptured and the cyst collapsed, and a considerable amount of colloid was seen outside the cyst. The lining epithelium of cyst was cubical, and the cells showed no granulation. There were a few small colloid cysts between the posterior wall of the main cyst and the posterior lobe of the pituitary (Plate I, g, h, Plate II, j, and fig. 3). The anterior lobe had a maximal antero-posterior diameter of 2·5 mm. Basophil cells were plentiful in all areas. In some areas the eosinophil cells were almost absent, while in other areas they were increased in number at the expense of chromophobe cells (compensatory hypertrophy: Berblinger, 1927).

THYMUS. There was atrophy of the thymus, with marked lipomatous metamorphosis.

THYROID. The vesicles were large and filled with a colloid which in some places showed a few large vacuoles, in other places numerous small vacuoles.

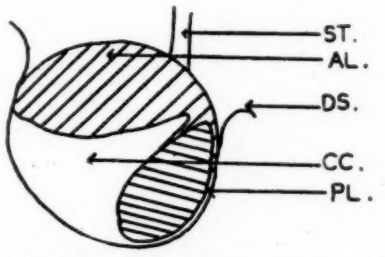

FIG. 3.—Schematic reconstruction of the immediate post-mortem findings on the pituitary in case 2. A.L. =anterior lobe; P.L.=posterior lobe; ST.=stalk; C.C.=colloid cyst; D.S.=dorsum sellae.

KIDNEY. The glomeruli showed a slight intracapillary hyalinization. The hyaline was present only in a few loops of the tuft, the majority of loops being widely patent. The first convoluted tubuli were markedly dilated and filled either with a pale, foamy material or with hyaline casts. The lining epithelium was cuboid or flat. Many of the epithelial cells showed large vacuoles (no fat stain made). A foamy material similar to that in the first convoluted tubuli was also seen in the Henle loops and in the collecting tubuli. The renal pelvis showed an epithelial proliferation, and in a few places a modified epithelium with the characters of a stratified squamous epithelium without cornification.

SPLEEN. The malpighian bodies were normal, the venous sinuses narrow, and Billroth's cords very cellular with numerous polymorphonuclear leucocytes.

PANCREAS. The interlobular connective tissue was considerably increased in amount. It consisted of fibroblasts, thick collagenous fibres, and numerous small round cells with an occasional polymorphonuclear leucocyte. This connective tissue invaded the individual lobules, which showed an advanced atrophy of the secretory tissue. They consisted of ducts, infundibuli, and small, usually crescent-shaped, groups of secretory cells attached to the tips of the infundibuli. The acinus cells were modified and more narrow than normal, and zymogen granules were absent. When they were isolated, it was often difficult to decide whether we had to deal with an acinus or a cross section of a duct. Between these parenchyma cells there was a large amount of loose connective tissue with patches of round-cell infiltration. Many of the inter- and intralobular ducts were markedly dilated and filled with an eosinophil homogenous or stratified material. In some places the latter showed a pale granular centre and a homogenous, intensely eosinophil

periphery; in other places the central part was homogenous and surrounded by several wavy layers of deeply eosinophil material, separated by almost colourless interspaces. In some of the larger dilated ducts, desquamated epithelial cells and a few inflammatory cells were enclosed in the eosinophil concretions. Some of the dilated ducts showed necrosis of the lining epithelium and were surrounded by connective tissue with dense cellular infiltration. The cellular infiltration was more marked in the head of the pancreas near to the duodenum than in the body and the tail. The main pancreatic duct was patent. Near to the papilla of Vater it was almost completely blocked by numerous eosinophil 'microliths,' fibrillary concretions, and desquamated epithelial cells. The islands of Langerhans were normal in number and appearance (Plate II, k and l).

DUODENUM. The duodenum showed a marked cellular infiltration of the mucosa which in a few places extended into the submucosa and which consisted of plasma cells, lymphocytes, and eosinophil leucocytes.

OVARY. There were several follicular cysts, 1·5 to 3 mm. in diameter, but otherwise nothing abnormal.

BONE MARROW. The bone marrow of the middle part of the femur consisted of fat tissue with islands of haematopoietic tissue. The latter showed numerous myelocytes, nucleated red blood corpuscles, and a few mature neutrophil leucocytes.

BONES. The rib and lower end of the femur were decalcified—the former completely, the latter partially. The proliferating zone proper of the cartilage and in a lesser degree the columnar zone were decreased in width. The provisional calcification zone was normal. In the zone of primary marrow formation, the longitudinal trabeculae of bone and calcified cartilage matrix were short and separated by wide and shallow bays. In some places there were, instead of the longitudinal, transverse bone trabeculae directly attached to the zone of provisional calcification. In the diaphysis the trabeculae were thin and widely separated, and showed osteoid seams which were, especially in the rib, markedly broader than normal. Fairly broad osteoid seams surrounded also the short trabeculae of calcified cartilage matrix. The bone marrow within the distal part of the femur was entirely fat marrow.

Summary of findings. A girl, eight years of age, died after five months' illness with severe wasting, muscular weakness, apathy, steatorrhoea, macrocytic hyperchromic anaemia, latent tetany, decrease of sodium and chlorides in the serum, and hypersensitiveness to insulin. The necropsy examination revealed a large colloid cyst of the pituitary, replacing Rathke's cleft, and a fibrocytic dystrophy of the pancreas. The child was 7 cm. shorter than the normal average, and the histological examination showed evidence of arrested growth (cf. Harris, 1933) associated with osteoporosis and mild rickets. The kidneys showed histological evidence of early glomerulo-nephritis.

Discussion

The two cases reported in this paper presented symptoms of progressive cachexia associated with muscular weakness and an apathetic state of mind. In one case there was an obvious, in the other a slight, stunting of growth. These symptoms were associated in the first case with symptoms of a lower motor neuron lesion. In the second case there was steatorrhoea, macrocytic hyperchromic anaemia, and metabolic changes suggestive of Addison's disease. Percortin treatment was, however, ineffective and this, together with an increased insulin-sensitiveness, pointed to disease of the pituitary or hypothalamus.

Necropsy in each case showed a large colloid cyst replacing the cleft of Rathke and causing atrophy of the anterior lobe. The cysts were lined by flat or cubical epithelium; there was no evidence of neoplastic growth. The absence of inflammatory changes or fibrosis, and the presence of an almost intact epithelial lining and of colloid in the cysts ruled out the possibility of the cysts being the result of a previous necrosis. There could, therefore, be no doubt that the origin of the cysts was over-secretion and retention of colloid. In this respect they resembled the pancreatic cysts studied by Wegelin (1921) and his pupil Yamane (1921), which were due to a developmental error, grew very slowly as a result of secretion and retention, and have, therefore, been met with almost exclusively in adults. They have sometimes been associated with the Lindau syndrome. Wegelin (1921) introduced the designation 'dysontogenetic retention cysts' for this type of cyst formation. The application of such an interpretation to the pituitary cysts is closely related to the problem of pituitary colloid. The original conception of its being the internal secretion of the pituitary was rejected by Erdheim (1926) Kraus (1926) and others, who saw in the colloid a useless waste product. Erdheim regarded the production of hypophyseal colloid as an atavistic rudimentary external secretion, Kraus as a product of colloid degeneration of anterior lobe cells. More recent investigations give support to the idea that the formation of colloid is linked with a part of the internal pituitary secretion. Guizzetti (1933) stressed the similarity between the lining cells of colloid cysts of the medullary zone on one hand, and the basophil cells of the anterior lobe on the other. Migration of basophil cells into the posterior lobe, and presence of a material, indistinguishable from the colloid of the medullary zone (Hering's 'hyaline bodies') in the posterior lobe and all the way towards the

hypothalamus, has been demonstrated by several authors (Kraus, 1926; Cushing, 1933; Benda, 1942; Selye, 1943). The inundation of hypothalamic centres with colloid is very marked after removal of the upper cervical sympathetic ganglion (Popjak, 1940). Selye (1943) has shown that intravenous injections of hypertonic NaCl-solutions into rats caused swelling of basophil cells in the anterior lobe of the pituitary gland, eventually with degenerative changes and at the same time considerable distension of Rathke's cleft with colloid. On the other hand the presence of symptoms of pituitary cachexia, of arrested growth, of suprarenal, testicular, and parathyroid changes in our two cases and in the case of Kiyono (1926), where a large amount of colloid was present in the cystic dilatation of Rathke's cleft, are strong evidence that the main hormones of the anterior pituitary lobe are not present in the colloid secretion. It is also worthy of note that in the two cases presented in this paper there was no evidence of colloid degeneration in the anterior lobe, and the whole amount of colloid was apparently the product of the epithelial lining of the cysts. It appears, therefore, conclusive (1) that the colloid is formed by both apocrine secretion of the lining cells of Rathke's cleft and by holocrine (possibly also apocrine) secretion of basophil cells of the anterior lobe; and (2) that the colloid formation is linked with only a part of pituitary hormone production, probably that associated with the activity of posterior lobe and the hypothalamic centres. The problem of ' neurocrine ' formation of colloid by pituicytes and the hypothalamus (Scharrer's (1941) diencephalic gland) is for our problem irrelevant.

In the present two cases the cleft of Rathke did not undergo the normal segregation into a series of small cysts; but instead, as a result of a continuous, increased colloid secretion by its lining epithelium, it became transformed into a large retention cyst, thus causing atrophy and hypofunction of the anterior lobe and an accumulation of a secretion which may have an influence on the hypothalamic centres.

As mentioned in the introduction, even comparatively large colloid cysts do not usually cause symptoms of hypo- or apituitarism. Why they do so in rare cases is still a debatable problem. It has been repeatedly assumed (Kiyono, 1926 ; Merz, 1930) that a separation of the anterior lobe from the posterior has similar effects to disease of the anterior lobe. In the first of the two cases described in this paper there was complete separation, but in the second a strip of anterior lobe tissue was seen closely attached to the superior pole of the neurohypophysis. Possibly the presence of pharyngeal hypophysis accounts for the fact that some large colloid cysts cause no clinical symptoms.

In the first case there was a marked atrophy of the testicles, morphological changes in the suprarenals, lipomatosis of at least one parathyroid, and syringomyelia of lumbar cord. The parathyroid changes are noteworthy because of the still contested formation of a parathyrotropic hormone by the anterior pituitary lobe (see Cameron, 1945; Perlman, 1944). The changes in the testicles, although very marked, occur also in other cases of undescended testicles (Kyrle, 1910). It is, however, possible, that these are also related to pituitary dysfunction, and according to Gruenwald (1946) they are less frequent than previously assumed and changes less marked than those found in the present case are considered by this author as evidence of underdevelopment. Syringomyelia is apparently an independent, associated condition. As syringomyelia is now considered by most authors to be a developmental error with persistence of primitive glia (Tamaki and Lubin, 1938), this association supports the interpretation of the pituitary cyst in the present case as ' dysontogenetic ' in origin. The slight gliosis and rarefaction at the floor of the fourth ventricle is apparently of the same nature as the cavity formation in the lumbar cord. There is no reason to associate the changes in the spinal cord of this case with the condition described as ' pseudotabes pituitaria ' (Otto, 1936; Snapper et al., 1937).

In the second case the colloid cyst of the pituitary was associated with atrophy and fibrocystic degeneration of the pancreas. The relationship of these two conditions can, in the present state of our knowledge, only be a matter of speculation. The possibility of a causal link between these diseases cannot, however, be disregarded. In a paper read before the Association of Clinical Pathologists it was pointed out (Baar, 1944) that what is now generally called ' fibrocystic disease of the pancreas ' comprises two pathogenetically different conditions. In very rare cases there is histological evidence that the cysts are due to segregation of ducts, pathological proliferation of their epithelium, and retention of a thin, mucoid, secreted material. This has been considered as the infantile form of the condition described by Wegelin (1921) and Yamane (1921) as ' dysontogenetic pancreatic cystosis.' Wissler and Zollinger (1945) recently came to the same conclusion. For the common form of the infantile fibrocystic disease of the pancreas, histological evidence has been presented to support the opinion of Blackfan and Wolbach (1933) and Blackfan and May (1938) that a pathological change in the secretion leading to its inspissation is the primary

change, resulting in stagnation of the secretion, cystic dilatation of ducts, infundibuli and acini, their secondary segregation, occasionally necrosis of the epithelium and rupture of ducts, atrophy of secretory tissue with inter- and intracinous fibrosis, and secondary inflammatory cellular infiltration. The present case belongs to this second type, for which the designation ' fibrocystic dystrophy of the pancreas ' was proposed. An attempt was made to explain these findings in a way which would do justice to the identical condition in the early neonatal period, which is invariably associated with either a meconium ileus or a congenital obliteration within the small intestine. A hypothesis was put forward that the primary cause is a disturbance in the balance between the autonomic and secretin stimuli in favour of the former. In the present case it is possible that the increased formation of pituitary colloid caused an increased stimulation of the posterior lobe and of the parasympathetic hypothalamic centres. It may be interesting in this connexion to observe that proliferative changes in the neurohypophysis have been actually described in Simmonds' disease (Jacob, 1923; Meng, 1928). The writer is fully aware of the hypothetical nature of the views presented but hopes that they may stimulate a more thorough investigation of faecal fats and of changes in the secretory pancreatic tissue in cases of pituitary disease.

The presence of a disturbance in the electrolytes resembling that in Addison's disease is of particular interest. Although hypophysectomy causes an atrophy of the suprarenal cortex, no change occurs in the blood sodium, chloride, or potassium levels (Swan, 1940). Cameron (1945) calls cases of Simmonds' disease with marked symptoms of hypocorticoadrenalism pituitary Addison's disease, but the writer is aware of only one case (Moss, 1942) in which changes in blood electrolytes similar to those in the present case were found.

The macrocytic hyperchromic anaemia in this case is probably due to the steatorrhoea and not directly to the pituitary disease. Snapper et al. described cases of hyperchromic anaemia and histamine-refractory achlorhydria in chronic pituitary insufficiency. They stress, however, the fact that the anaemia was a late symptom in the course of the disease and developed only after achlorhydria was present for a considerable period. The hypocalcaemia and latent tetany have also their reasonable explanation in the pancreatic steatorrhoea and formation of excess calcium soaps in the intestine. The blood was not examined in the first case, but the presence of haemosiderosis and extramedullary haematopoiesis are evidence of a haemolytic anaemia.

With regard to the histogenesis of the two pituitary cysts, there can be but little doubt that they are due to a developmental error. There is not the slightest evidence of neoplastic growth. Both cysts have developed in a position where in embryonic life there is a flat cavity, the ' primary Rathke's cyst.' Instead of becoming rudimentary, changing into the Rathke's cleft and finally segregating into a few small ' secondary Rathke's cysts,' in these cases the lining epithelium continued to grow as such, and to produce a colloid secretion which accumulated and caused the formation of a cyst gradually increasing in size. In analogy with the nomenclature of Wegelin mentioned above, the designation ' dysontogenetic pituitary cysts ' for this type and the following classification of pituitary cysts is, therefore, suggested.

1. Neoplastic (cystic craniopharyngeoma, the most common form among the pathological cysts of the pituitary, and very occasionally adenoma with cystic degeneration).

2. Dysontogenetic (pathological colloid cysts and ciliated epithelial cysts, cases of Goldzieher, Kiyono, Frazier and Alpers and the present two cases, and ? Merz's first case).

3. Dystrophic (due to embolism or thrombosis followed by necrosis and cystic degeneration: Falta, 1913 ; Simmonds, 1919 ; ? Merz, 1930).

4. A combination of 2 and 3 (the only case of this type has been described by Priesel in 1920. In this case a developmental dystopy of the pituitary caused a defective nutrition with secondary cyst formation and symptoms of pituitary dwarfism).

5. Combination of 2 and 1 (this is represented by the remarkable case of Worster-Drought et al., 1927). In a girl aged nineteen with pituitary dwarfism, three ciliated epithelial cysts were found, and a neoplastic growth arising from the primitive epithelium of Rathke's cyst or from the ependyma of the third ventricle (? Duffy's fourth case).

Summary

Two cases of pituitary cachexia in childhood are described. Both were due to large colloid cysts of Rathke's cleft with pressure atrophy of the anterior lobe. The designation ' dysontogenetic pituitary cysts ' for this type, and a classification of the various pituitary cysts are proposed. The reasons are pointed out why the designation ' tumours of Rathke's pouch ' for carniapharyngeomata is considered to be a misnomer. The pituitary cachexia was associated with syringomyelia in one case and with fibrocystic dystrophy of the pancreas in the other. The possibility of a causal link between the latter and the pituitary disease is discussed.

It is my pleasant duty to thank Sir Leonard G. Parsons for his helpful criticism and advice; Professor K. D. Wilkinson and Dr. A. V. Neale for permission to publish their cases, Mr. A. R. Detheridge for cutting and staining the sections, and Mr. J. Gregory Williamson for the photographs.

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REVIEWS

Die Scheuermannsche Krankheit. By J. E. W. BROCHER, dozent in the University of Geneva. Basel, Benno Schwabe. 1946. Pp. 91. (Price, Fr. 11.)

This monograph is more than a description of adolescent kyphosis. The 122 illustrations with their short case histories cover the whole field of disc pathology.

As a disciple of Schmorl, Dr. Brocher has tried to correlate the radiological signs of disc pathology with clinical symptoms, and he has produced an interesting study of Scheuermann's disease. He rightly stresses the frequency with which this apparently benign disease gives rise to chronic pain and disability in later life, as result of arthritic changes in the mobile segments of the spine above and below the immobile and painless kyphos. The less common but more disabling lumbar form of the disease is given the prominence it deserves. The relation of trauma to back pain in adults with x-ray signs of old disease are discussed in detail, and he lays down rules for guidance in compensation cases. On etiology Dr. Brocher has little new to offer. He believes that weak back muscles, the trauma of heavy work, and some constitutional defect of the spine, all play their part in producing the characteristic wedging of vertebral bodies. Unfortunately, he has not been able to make any survey of children in the presymptomatic stage; nor can he provide any information about the nature of the constitutional defect.

Treatment is on routine lines: rest in recumbency, exercises for the back muscles, and protection from heavy work during the active stage of the disease.

This monograph deals largely with the late results of Scheuermann's disease in adults and a careful study has been made of the symptoms of associated osteo-arthritis. This in itself is interesting, but one would like to hear more about etiology and prevention of the condition at its inception in childhood.

The Psycho-Analytical Treatment of Children: Technical Lectures and Essays. By ANNA FREUD. Parts I and II, translated from the German by Nancy Procter-Gregg. London, Imago Publishing Co., Ltd., 1946. Pp. 98. (Price 10*s.* 6*d.*)

This is essentially a work for the practising analyst, but is so clearly written that it is likely to be of interest to others concerned with any branch of child psychology. It is the fruit of wide personal experience, and the flexibility of the author's technique is illustrated from the handling of a number of protracted child analyses. The author stresses the different methods of approach necessary in dealing with children as compared with adult subjects of analysis, and how some of these, whilst differing widely from the orthodox adult technique, may serve to attain a similar purpose.

The Care of Young Babies. By JOHN GIBBENS, M.D., M.R.C.P., Medical Officer to the Babies' Club, Chelsea. With a Foreword by Sir Robert Hutchison, Bt., M.D., F.R.C.P., Ex-President of the Royal College of Physicians. London, J. and A. Churchill, Ltd. Second edition, 1946. Pp. 200. With 7 plates and 7 text-figures. (Price 5*s.*)

The first edition of this useful little book has had five reprintings since it was published in 1940, and the second has now been revised and expanded. Written in a breezy, colloquial style, it contains in its two hundred pages a surprising amount of information. There can be no doubt that there is a place for a book of this kind, and, as it contains little that is controversial, it can be cordially recommended for family reading.

Clinical Practice in Infectious Diseases: For students, practitioners and medical officers. By E. H. R. HARRIES, M.D.Lond., F.R.C.P., Medical Superintendent, North Eastern Hospital (L.C.C.), and M. MITMAN, M.D.Lond., F.R.C.P., Medical Superintendent, River Hospitals. With a Foreword by Sir Allen Daley, M.D.Lond., F.R.C.P., Medical Officer of Health, London County Council. Third edition. Edinburgh, E. and S. Livingstone, Ltd. 1947. Pp. 679. (Price 22*s.* 6*d.*)

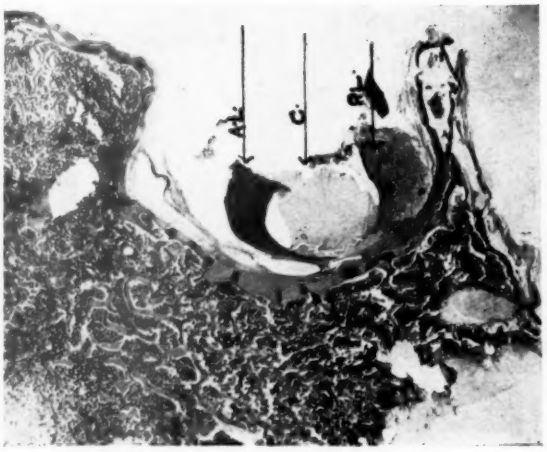
The appearance of a third edition of this deservedly popular work is most welcome, as it has unavoidably been out of print for over a year. The whole book has been revised and much new material added, bringing it into line with the advances in treatment which have occurred since 1943. It is already a standard work, and is likely to remain so. The production retains the high quality which the publishers have led us to expect of them.

The following have also been received:

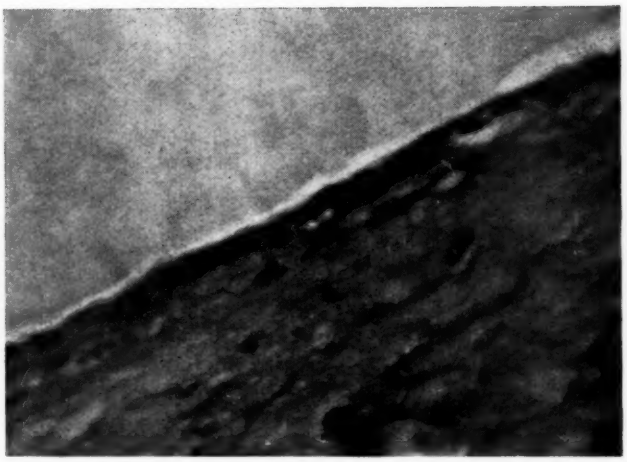
Chemotherapeutic and other Studies of Typhus. By M. VAN DEN ENDE, C. H. STUART-HARRIS, F. FULTON and J. S. F. NIVEN, with C. H. ANDREWES, A. M. BEGG, W. J. ELFORD, M. H. GLEESON WHITE, W. L. HAWLEY, K. C. MILLS, F. HAMILTON, and C. C. THOMAS. M.R.C., Spec. Rep. Series, No. 255. London. H.M.S.O. 1946. Pp. 246. (Price 12*s.* 6*d.*)

The Cultivation of Viruses and Rickettsiae in the Chick Embryo. By W. I. B. BEVERIDGE and F. M. BURNET. M.R.C., Spec. Rep. Series, No. 256. London. H.M.S.O. 1946. Pp. 92. (Price 2*s.*)

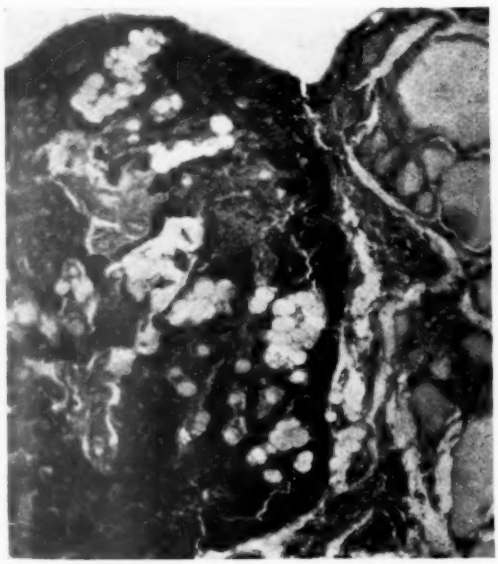
A Synopsis of Orthopaedic Surgery. By A. DAVID LE VAY, M.S.Lond., F.R.C.S.Eng., Honorary Orthopaedic Surgeon, Woolwich Memorial Hospital. With 55 illustrations. London. H. K. Lewis and Co., Ltd. 1947. Pp. 242. (Price 15*s.*)



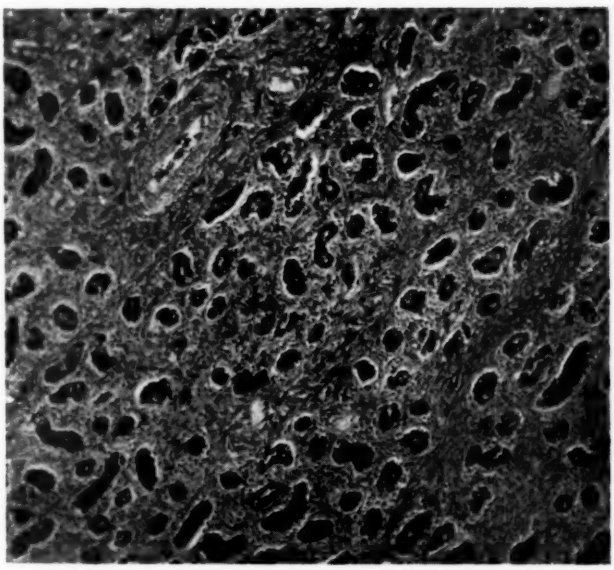
(a). Midsagittal section of the sella turcica with the pituitary cyst in case 1. The cyst shows considerable shrinkage. Originally the cyst with the posterior and the atrophic anterior lobes filled the whole sella. A.L.=anterior lobe; C=colloid cyst; P.L.=posterior lobe. H.E., × 4.



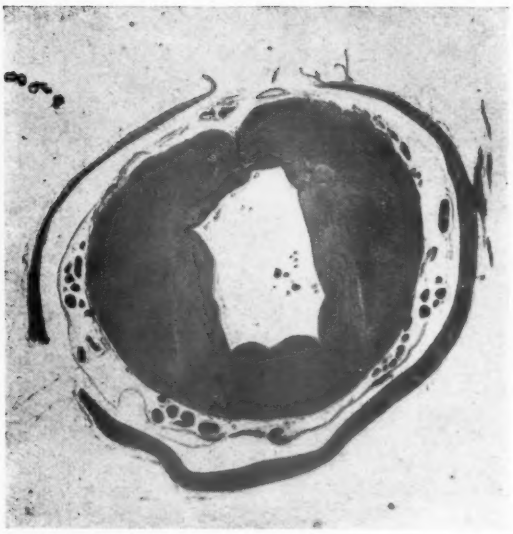
(b). Posterior wall of the cyst in case 1. H.E., × 670.



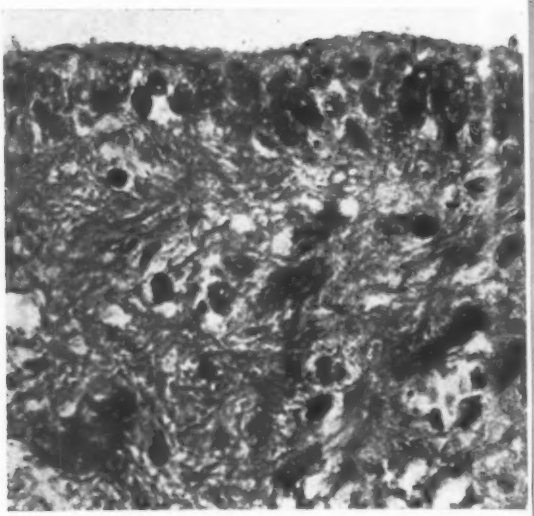
(c). Part of the thyroid and a parathyroid in case 1, showing lipomatosis of the latter. H.E., × 65.



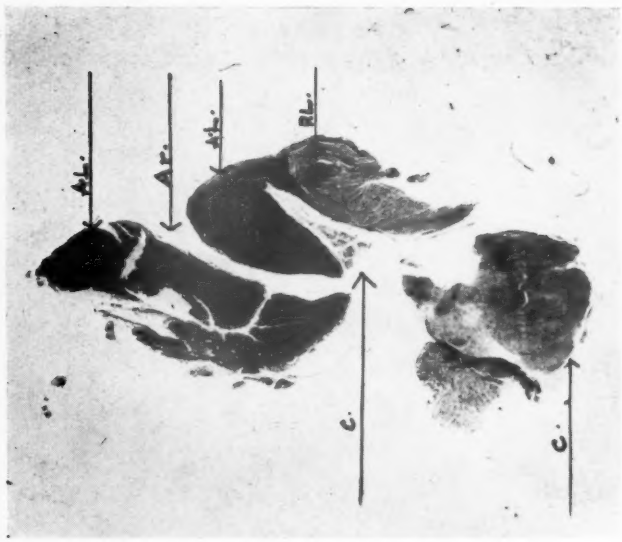
(d). Testicle in case 1. H.E., × 65.



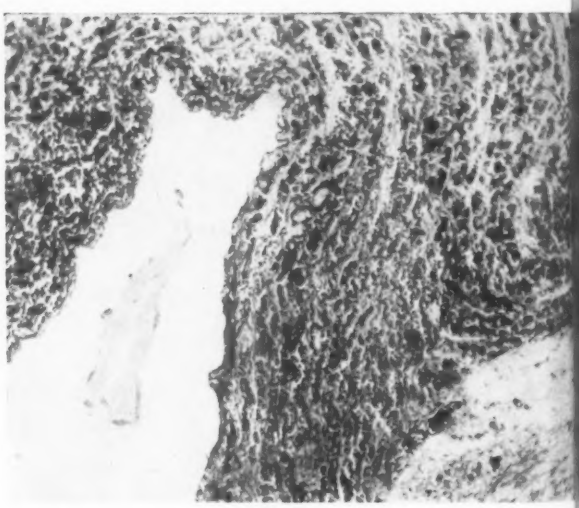
(e). Cross section of the lumbar cord in case 1, showing the central cavity. H.E., × 4.



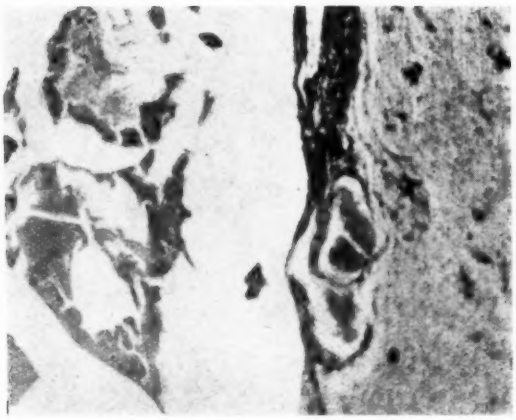
(f). Part of the wall of the cavity in the lumbar cor of case 1. This part is lined by ependyma and surrounde by an area of dense gliosis. Mallory's phospho tungstic acid-haematoxylin. × 670.



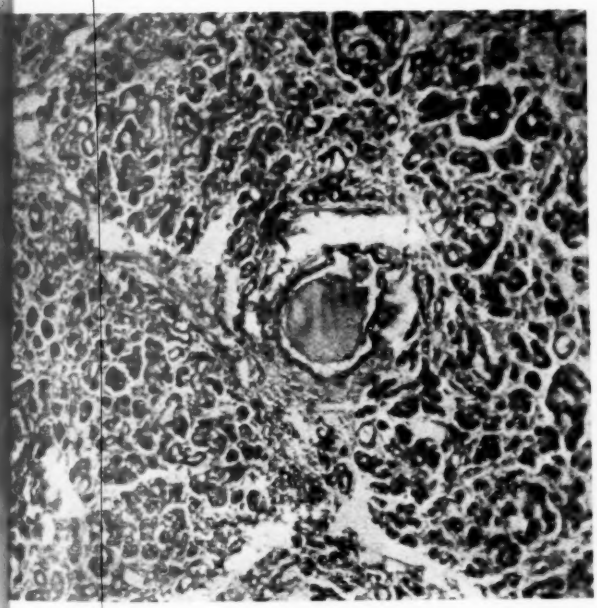
(g). Midsagittal section of the pituitary in case 2. The cyst is ruptured and collapsed, most of the colloid is outside the cavity of the cyst. A.L.=anterior lobe; P.L.=posterior lobe; Ar=artifact; c=colloid. H.E., × 4.



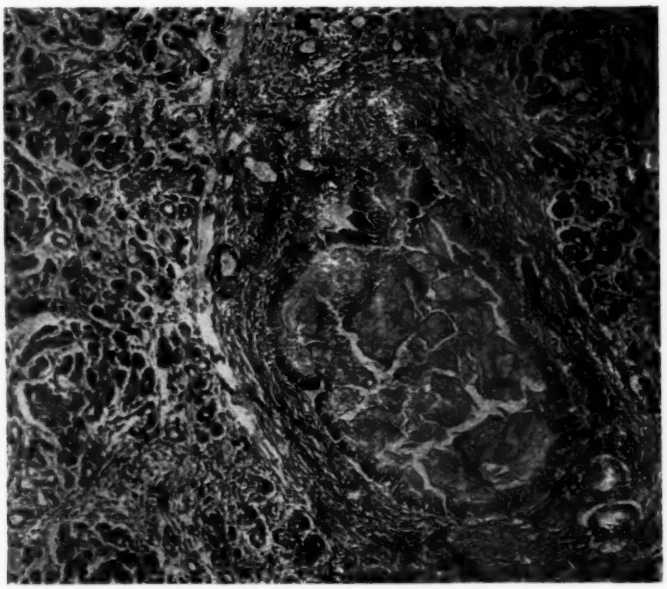
(h). Upper part of Rathke's cleft in case 2. H.E., ×



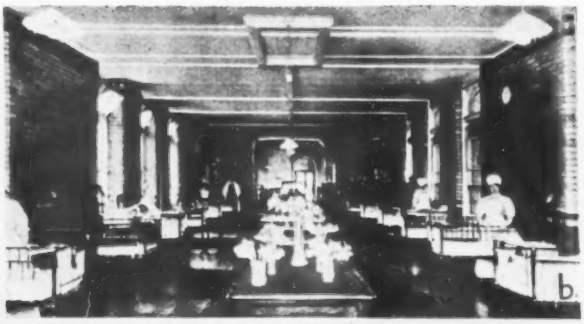
(j). Middle part of the cystically dilated Rathke's cleft in case 2, with colloid in the cavity, and two small colloid cysts on the anterior aspect of the posterior lobe (secondary Rathke's cysts). H.E., × 85.

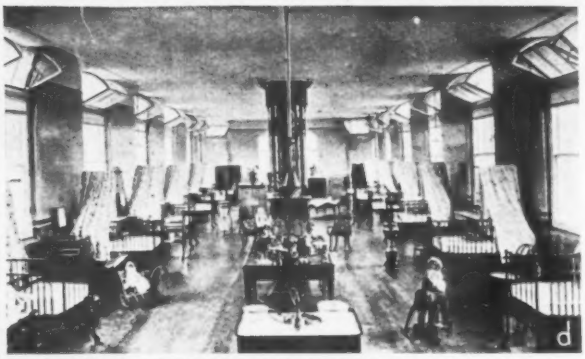


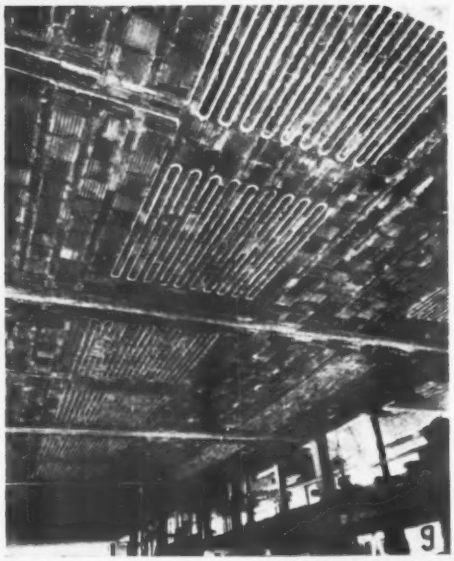
(k). Fibrocystic dystrophy of the pancreas in case 2. H.E., × 85.

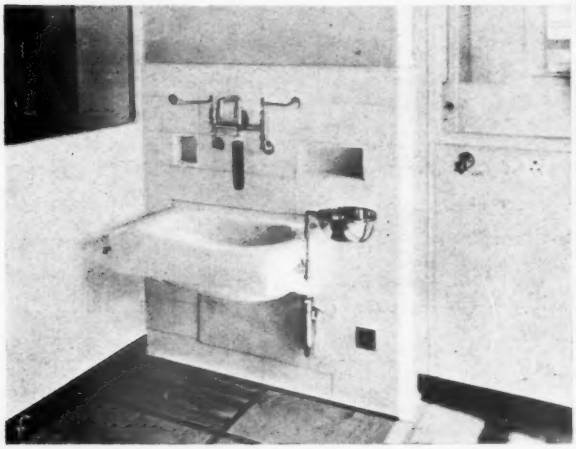


(l). Fibrocystic dystrophy of the pancreas in case 2. H.E., × 85.









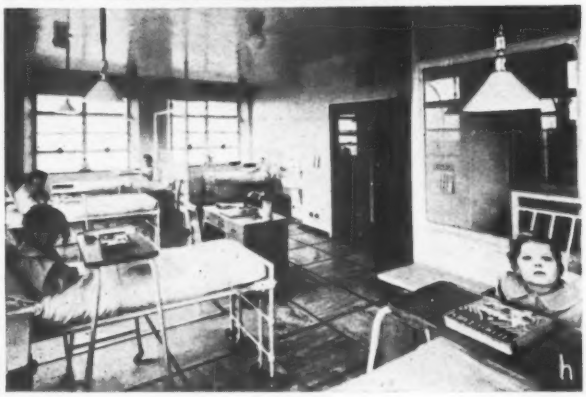
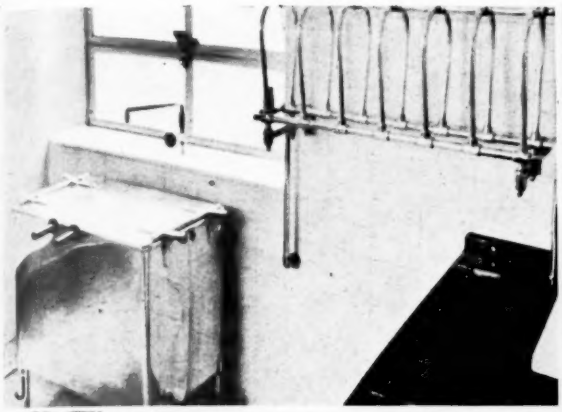
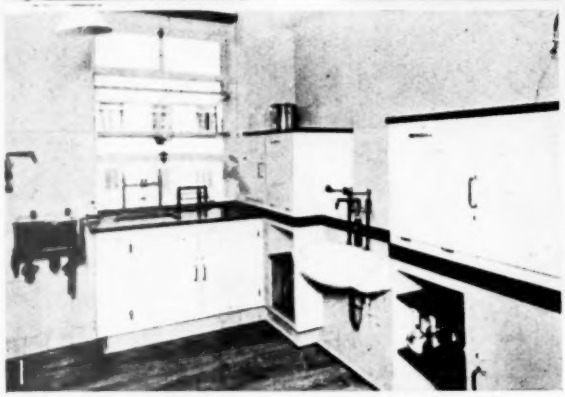
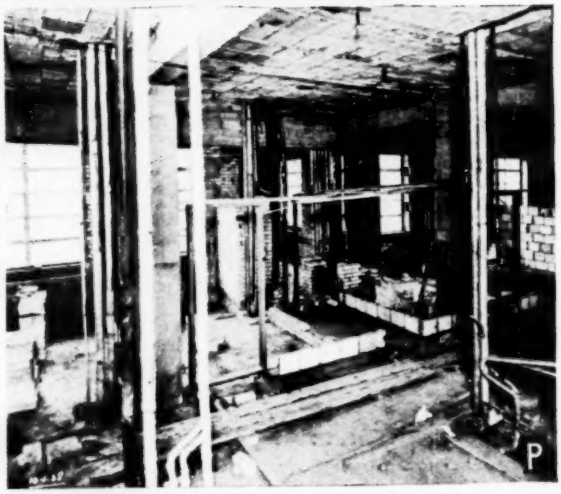
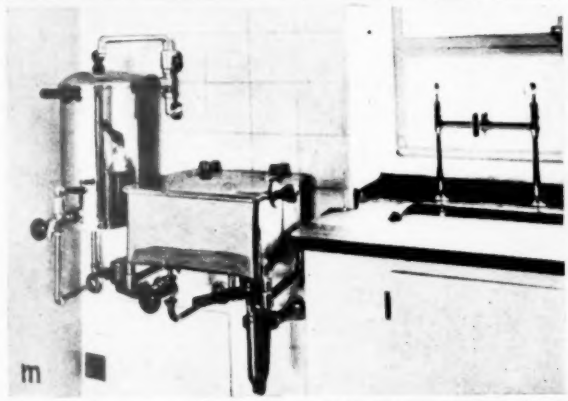


PLATE III









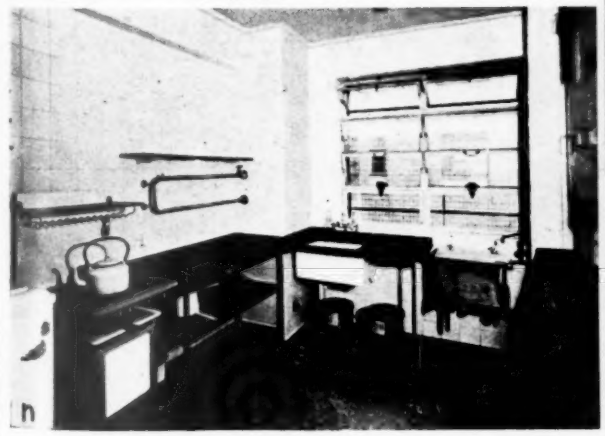


PLATE IV


The Operating Theatre
Hospital for Sick Children
Great Ormond Street, W.C.
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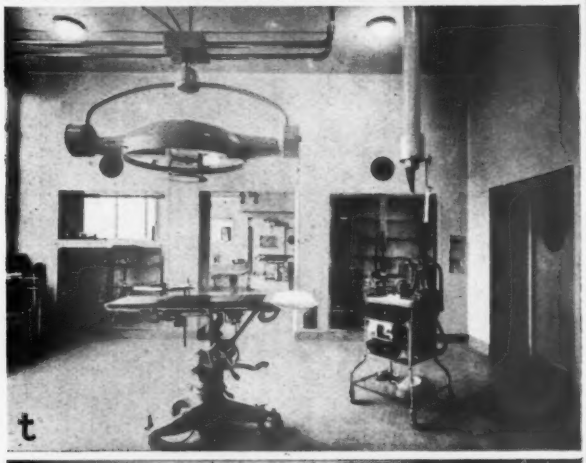
t


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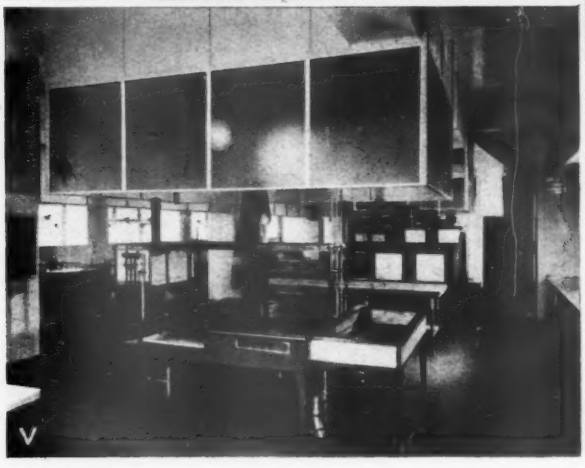
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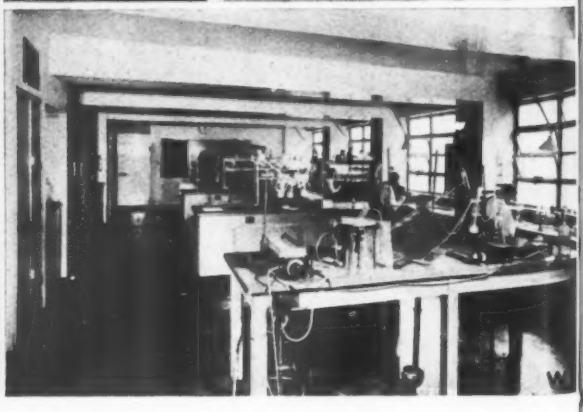
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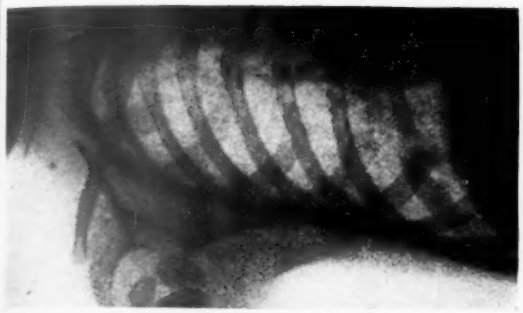
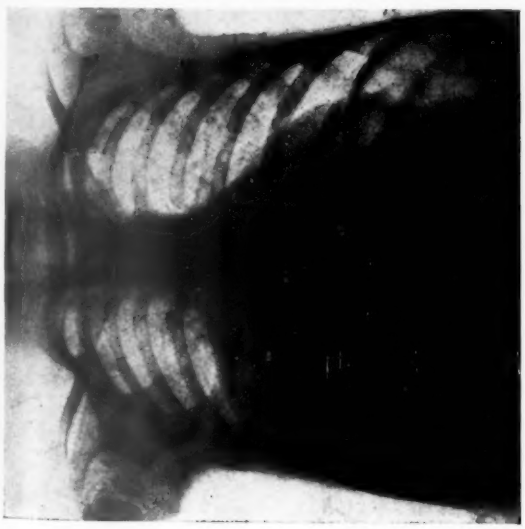
PLATE V



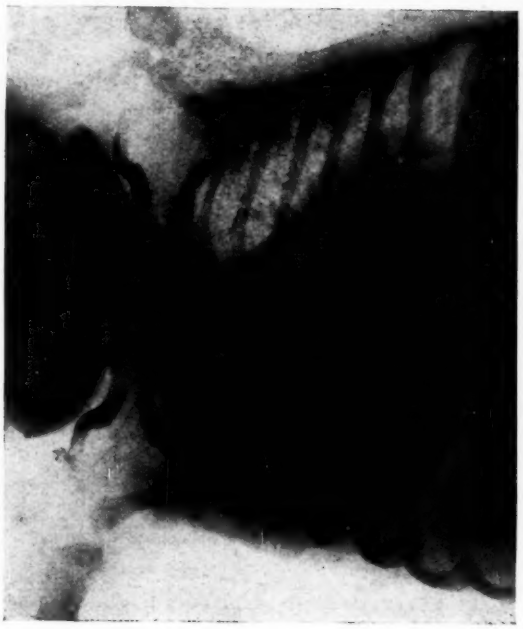
(c).—Case 3, final radiograph.

(b)—Case 3, immediate post-operative state.

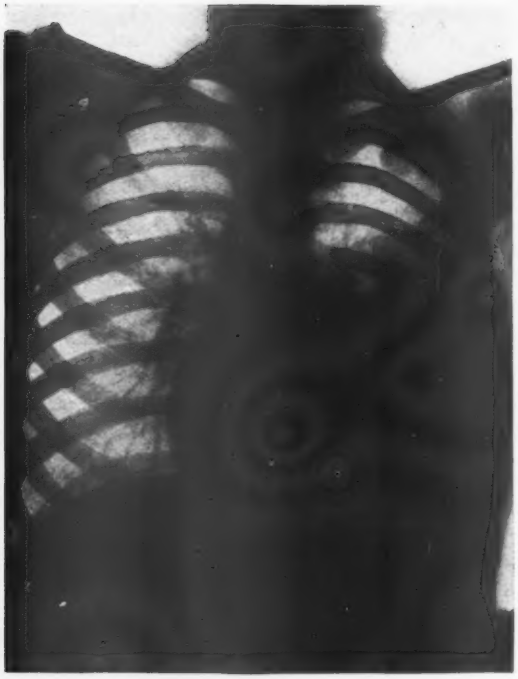


(a)—Case 3, before penicillin therapy.

(e)—Case 6, final radiograph after aspiration only.

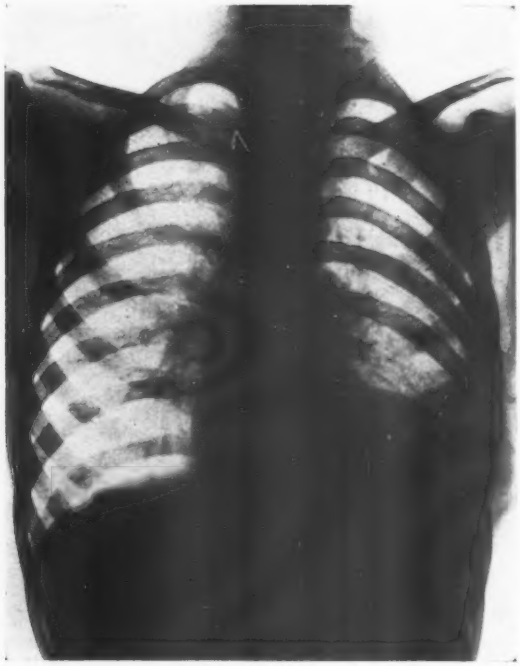


(d)—Case 6, before penicillin therapy.



(a)—Case 11, before penicillin therapy.

(b)—Case 11, after penicillin without resolution.



(c)—Case 11, after surgical drainage.

PLATE VII